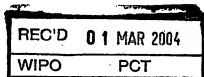


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**Prioritätsbescheinigung über die Einreichung
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Bezeichnung: Method and nucleic acids for the improved treatment of breast cell proliferative disorders

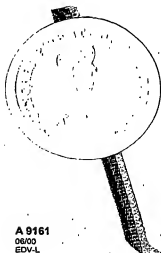
IPC: C 12 Q 1/68

Die angehefteten Stücke sind eine richtige und genaue Wiedergabe der ursprünglichen Unterlagen dieser Patentanmeldung.

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Method and nucleic acids for the improved treatment of breast cell proliferative disorders

Field of the Invention

The levels of observation that have been studied by the methodological developments of recent years in molecular biology, are the genes themselves, the translation of these genes into RNA, and the resulting proteins. The question of which gene is switched on at which point in the course of the development of an individual, and how the activation and inhibition of specific genes in specific cells and tissues are controlled is correlatable to the degree and character of the methylation of the genes or of the genome. In this respect, pathogenic conditions may manifest themselves in a changed methylation pattern of individual genes or of the genome.

DNA methylation plays a role, for example, in the regulation of the transcription, in genetic imprinting, and in tumourigenesis. Therefore, the identification of 5-methylcytosine as a component of genetic information is of considerable interest. However, 5-methylcytosine positions cannot be identified by sequencing since 5-methylcytosine has the same base pairing behaviour as cytosine. Moreover, the epigenetic information carried by 5-methylcytosine is completely lost during PCR amplification.

A relatively new and currently the most frequently used method for analysing DNA for 5-methylcytosine is based upon the specific reaction of bisulfite with cytosine which, upon subsequent alkaline hydrolysis, is converted to uracil which corresponds to thymidine in its base pairing behaviour. However, 5-methylcytosine remains unmodified under these conditions. Consequently, the original DNA is converted in such a manner that methylcytosine, which originally could not be distinguished from cytosine by its hybridisation behaviour, can now be detected as the only remaining cytosine using "normal" molecular biological techniques, for example, by amplification and hybridisation or sequencing. All of these techniques are based on base pairing which can now be fully exploited. In terms of sensitivity, the prior art is defined by a method which encloses the DNA to be analysed in an agarose matrix, thus preventing the diffusion and renaturation of the DNA (bisulfite only

reacts with single-stranded DNA), and which replaces all precipitation and purification steps with fast dialysis (Olek A, Oswald J, Walter J. A modified and improved method for bisulphite based cytosine methylation analysis. *Nucleic Acids Res.* 1996 Dec 15;24(24):5064-6). Using this method, it is possible to analyse individual cells, which illustrates the potential of the method. However, currently only individual regions of a length of up to approximately 3000 base pairs are analysed, a global analysis of cells for thousands of possible methylation events is not possible. However, this method cannot reliably analyse very small fragments from small sample quantities either. These are lost through the matrix in spite of the diffusion protection.

An overview of the further known methods of detecting 5-methylcytosine may be gathered from the following review article: Rein, T., DePamphilis, M. L., Zorbas, H., *Nucleic Acids Res.* 1998, 26, 2255.

To date, barring few exceptions (e.g., Zeschnick M, Lich C, Buiting K, Doerfler W, Horsthemke B. A single-tube PCR test for the diagnosis of Angelman and Prader-Willi syndrome based on allelic methylation differences at the SNRPN locus. *Eur J Hum Genet.* 1997 Mar-Apr;5(2):94-8) the bisulfite technique is only used in research. Always, however, short, specific fragments of a known gene are amplified subsequent to a bisulfite treatment and either completely sequenced (Olek A, Walter J. The pre-implantation ontogeny of the H19 methylation imprint. *Nat Genet.* 1997 Nov;17(3):275-6) or individual cytosine positions are detected by a primer extension reaction (Gonzalzo ML, Jones PA. Rapid quantitation of methylation differences at specific sites using methylation-sensitive single nucleotide primer extension (Ms-SNuPE). *Nucleic Acids Res.* 1997 Jun 15;25(12):2529-31, WO 95/00669) or by enzymatic digestion (Xiong Z, Laird PW. COBRA: a sensitive and quantitative DNA methylation assay. *Nucleic Acids Res.* 1997 Jun 15;25(12):2532-4). In addition, detection by hybridisation has also been described (Olek et al., WO 99/28498).

Further publications dealing with the use of the bisulfite technique for methylation detection in individual genes are: Grigg G, Clark S. Sequencing 5-methylcytosine residues in genomic DNA. *Bioessays.* 1994 Jun;16(6):431-6, 431; Zeschnick M, Schmitz B, Dittrich B, Buiting K, Horsthemke B, Doerfler W. Imprinted segments in the human genome: different DNA methylation patterns in the Prader-Willi/Angelman syndrome region as determined by the genomic sequencing method. *Hum Mol Genet.* 1997 Mar;6(3):387-95; Feil R, Charlton J,

Bird AP, Walter J, Reik W. Methylation analysis on individual chromosomes: improved protocol for bisulphite genomic sequencing. *Nucleic Acids Res.* 1994 Feb 25;22(4):695-6; Martin V, Ribieras S, Song-Wang X, Rio MC, Dante R. Genomic sequencing indicates a correlation between DNA hypomethylation in the 5' region of the pS2 gene and its expression in human breast cancer cell lines. *Gene.* 1995 May 19;157(1-2):261-4; WO 97/46705, WO 95/15373, and WO 97/45560.

An overview of the Prior Art in oligomer array manufacturing can be gathered from a special edition of *Nature Genetics* (*Nature Genetics Supplement*, Volume 21, January 1999), published in January 1999, and from the literature cited therein.

Fluorescently labelled probes are often used for the scanning of immobilised DNA arrays. The simple attachment of Cy3 and Cy5 dyes to the 5'-OH of the specific probe are particularly suitable for fluorescence labels. The detection of the fluorescence of the hybridised probes may be carried out, for example via a confocal microscope. Cy3 and Cy5 dyes, besides many others, are commercially available.

Matrix Assisted Laser Desorption Ionization Mass Spectrometry (MALDI-TOF) is a very efficient development for the analysis of biomolecules (Karas M, Hillenkamp F. *Laser desorption ionization of proteins with molecular masses exceeding 10,000 daltons.* *Anal Chem.* 1988 Oct 15;60(20):2299-301). An analyte is embedded in a light-absorbing matrix. The matrix is evaporated by a short laser pulse thus transporting the analyte molecule into the vapour phase in an unfragmented manner. The analyte is ionised by collisions with matrix molecules. An applied voltage accelerates the ions into a field-free flight tube. Due to their different masses, the ions are accelerated at different rates. Smaller ions reach the detector sooner than bigger ones.

MALDI-TOF spectrometry is excellently suited to the analysis of peptides and proteins. The analysis of nucleic acids is somewhat more difficult (Gut I G, Beck S. *DNA and Matrix Assisted Laser Desorption Ionization Mass Spectrometry. Current Innovations and Future Trends.* 1995, 1; 147-57). The sensitivity to nucleic acids is approximately 100 times worse than to peptides and decreases disproportionally with increasing fragment size. For nucleic acids having a multiply negatively charged backbone, the ionization process via the matrix is considerably less efficient. In MALDI-TOF spectrometry, the selection of the matrix plays an

eminently important role. For the desorption of peptides, several very efficient matrixes have been found which produce a very fine crystallization. There are now several responsive matrixes for DNA, however, the difference in sensitivity has not been reduced. The difference in sensitivity can be reduced by chemically modifying the DNA in such a manner that it becomes more similar to a peptide. Phosphorothioate nucleic acids in which the usual phosphates of the backbone are substituted with thiophosphates can be converted into a charge-neutral DNA using simple alkylation chemistry (Gut IG, Beck S. A procedure for selective DNA alkylation and detection by mass spectrometry. Nucleic Acids Res. 1995 Apr 25;23(8):1367-73). The coupling of a charge tag to this modified DNA results in an increase in sensitivity to the same level as that found for peptides. A further advantage of charge tagging is the increased stability of the analysis against impurities which make the detection of unmodified substrates considerably more difficult.

Genomic DNA is obtained from DNA of cell, tissue or other test samples using standard methods. This standard methodology is found in references such as Fritsch and Maniatis eds., Molecular Cloning: A Laboratory Manual, 1989.

Breast cancer is currently the second most common type of cancer amongst women: In 2001 over 190,000 new cases of invasive breast cancer and over 47, 000 additional cases of *in situ* breast cancer were diagnosed. Incidence and death rates increase with age, for the period 1994 - 1998 the incidence of breast cancer amongst women between the ages of 20 and 24 was only 1.5 per 100,000 population. However the risk increases to 489.7 within the age group 75 - 79. Mortality rates have decreased by approximately 5% over the last decade and factors affecting 5 year survival rates include age, stage of cancer, socioeconomic factors and race.

Breast cancer is defined as the uncontrolled proliferation of cells within breasts tissues. Breasts are comprised of 15 to 20 lobes joined together by ducts. Cancer arises most commonly in the duct, but is also found in the lobes with the rarest type of cancer termed inflammatory breast cancer.

It will be appreciated by those skilled in the art that there exists a continuing need to improve methods of early detection, classification and treatment of breast cancers. In contrast to the detection of some other common cancers such as cervical and dermal there are inherent difficulties in classifying and detecting breast cancers.

The first step of any treatment is the assessment of the patient's condition comparative to defined classifications of the disease. However the value of such a system is inherently dependant upon the quality of the classification. Breast cancers are staged according to their size, location and occurrence of metastasis. Methods of treatment include the use of surgery, radiation therapy, chemotherapy and endocrine therapy, which are also used as adjuvant therapies to surgery.

Endocrine therapies have been developed in order to block the effects of estrogen on cancer cells or to reduce serum estrogen levels. Tamoxifen (TAM) is the most widely used antioestrogenic drug for breast cancer patients. It acts blocking estrogen stimulation of breast cancer cells, inhibiting both translocation and nuclear binding of estrogen receptor. TAM is used in adjuvant setting for primary breast cancer patients and for the treatment of metastatic disease and its effectiveness has been proved in several clinical trials. Treatment for five years reduces annual disease recurrence by 47% and annual deaths by 26% and this reduction is similar in different age groups. Also it reduces the incidence of developing contralateral breast tumours. TAM is among the least toxic antineoplastic agents but as it has estrogenic properties in some tissues, it increases by 3 folds the risk of endometrial cancer. Other endocrine therapies include aromatase inhibitors, which block the enzyme aromatase in adipose tissue (the main source of estrogen in postmenopausal women) and lead to reduced or abolished production of estrogens in adipose tissue. Also, new agents which block or modulate the estrogen receptor have been developed, they are generally summarised as SERMs = selective estrogen receptor modulators. Yet another way to reduce the amount of estrogen available to the tumour is to apply agents which interrupt the feed-back loop in sex hormone regulation (LH-RH analogues) at a higher level.

In general, the side-effects of endocrine treatment are harmless compared to chemotherapy. However, as endocrine treatments eliminate or reduce estrogen as a growth factor for cancer, they work only for tumours which rely on estrogen as a growth factor. The growth of cancers which do not have a functional ER pathway cannot be modulated by endocrine therapies.

The current way to determine if a tumour will respond to endocrine therapies is the analysis of expression of hormone receptors. Hormone receptor status should be tested prior to any endocrine treatment as only a group of patients will benefit from therapy. For this purpose ER

(estrogen receptor) and PR (progesterone receptor) status are tested routinely in all patients and they are considered predictive markers of response (a predictive marker or factor is any measurement associated with response or lack of response to a particular therapy). ER status is predictive of response in adjuvant endocrine therapy setting and also in advanced metastatic disease.

Currently, ER positive and or PR positive patients receive TAM and the remaining 10% of patients receive chemotherapy. The problem is that the endocrine treatment is only effective in a subgroup of hormone receptor positive patients and also, that a small subgroup of ER negative patients appear initially to respond to TAM. Then, the non responder subgroup will not only not benefit from endocrine treatment but have the adverse effects of it and will not have the opportunity to receive chemotherapy instead. On the other hand, the ER negative subgroup that could have benefit from endocrine treatment will receive instead chemotherapy. Several different assays are available to measure PR and ER, including biochemical and IHC (immunohistochemical) analysis, but there is a lack of standardisation of staining methods and interlaboratory variability (Clin Cancer Res 2000, 6:616-621).

Currently several predictive markers are under evaluation. As up to now most patients have received Tamoxifen as endocrine treatment most of the markers have been shown to be associated with response or resistance to tamoxifen. However, it is generally assumed that there is a large overlap between responders to one or the other endocrine treatment. In fact, ER and PR expression are used to select patients for any endocrine treatment. Among the markers which have been associated with TAM response is bcl-2. High bcl-2 levels showed promising correlation to TAM therapy response in patients with metastatic disease and prolonged survival and added valuable information to ER negative patient subgroup (J Clin Oncology 1997, 15 5:1916-1922; Endocrine, 2000, 13(1):1-10). There is conflicting evidence regarding the independent predictive value of c-erbB2 (Her2/neu) over expression in patients with advance breast cancer that require further evaluation and verification (British J of Cancer, 1999, 79 (7/8):1220-1226; J Natl Cancer Inst, 1998, 90 (21): 1601-1608).

Other predictive markers include SRC-1 (steroid receptor coactivator-1), CGA gene over expression, cell kinetics and S phase fraction assays (Breast Cancer Res and Treat, 1998, 48:87-92; Oncogene 2001, 20:6955-6959). Recently, uPA (Urokinase-type plasminogen activator) and PAI-1 (Plasminogen activator inhibitor type 1) together showed to be useful to

define a subgroup of patients who have worse prognosis and who would benefit from adjuvant systemic therapy (J Clinical Oncology, 2002, 20 n° 4). All of these markers need further evaluations in prospective trials as none of them is yet a validated marker of response.

- 5 A number of cancer-associated genes have been shown to be inactivated by hypermethylation of CpG islands during breast tumourigenesis. Decreased expression of the calcium binding protein S100A2 (Accession number NM_005978) has been associated with the development of breast cancers. Hypermethylation of the promoter region of this gene has been observed in neoplastic cells thus providing evidence that S100A2 repression in tumour cells is mediated by site-specific methylation.

- 10 The SYK gene (Accession number NM_003177) encodes a protein tyrosine kinase, Syk (spleen tyrosine kinase), that is highly expressed in hematopoietic cells. Syk is expressed in normal breast ductal epithelial cells but not in a subset of invasive breast carcinoma. Also, the loss of Syk expression seems to be associated with malignant phenotypes such as increased motility and invasion. The loss of expression occurs at the transcriptional level, and, as indicated by Yuan Y, Mendez R, Sahin A and Dai JL (Hypermethylation leads to silencing of the SYK gene in human breast cancer. Cancer Res. 2001;61(14):5558-61.), as a result of DNA hypermethylation.

- 20 The TGF- β type 2 receptor (encoded by the TGFBR2 gene, NM_003242) plays a role in trans-membrane signalling pathways via a complex of serine/threonine kinases. Mutations in the gene have been detected in some primary tumours and in several types of tumour-derived cell lines, including breast (Lucke CD, Philpott A, Metcalfe JC, Thompson AM, Hughes-Davies L, Kemp PR, Hesketh R. Inhibiting mutations in the transforming growth factor beta type 2 receptor in recurrent human breast cancer. Cancer Res. 2001 Jan 15;61(2):482-5).

- 30 The genes COX7A2L and GRIN2D were both identified as novel estrogen responsive elements by Watanabe et. al. (Isolation of estrogen-responsive genes with a CpG island library. Molec. Cell. Biol. 18: 442-449, 1998.) using the CpG-GBS (genomic binding site) method. The gene COX7A2L (Accession number NM_004718 encodes a polypeptide 2-like cytochrome C oxidase subunit VIIA. Northern blot analysis detected an upregulation of COX7A2L after estrogen treatment of a breast cancer cell line. The gene GRIN2D (Accession number NM_000836) encodes the N-methyl-D-aspartate, ionotropic, subunit 2D glutamate

receptor, a subunit of the NMDA receptor channels associated with neuronal signalling, furthermore expression of the cDNA has been observed in an osteosarcoma cell line. The gene VTN (also known as Vitronectin Accession number NM_000638) encodes a 75-kD glycoprotein (also called serum spreading factor or complement S-protein) that promotes attachment and spreading of animal cells in vitro, inhibits cytolysis by the complement C5b-9 complex, and modulates antithrombin III-thrombin action in blood coagulation. Furthermore expression of this gene has been linked to progression and invasiveness of cancer cells.

The gene SFN (also known as Stratifin) encodes a polypeptide of the 14-3-3 family, 14-3-3 sigma. The 14-3-3 family of proteins mediates signal transduction by binding to phosphoserine-containing proteins. Expression of the SFN gene is lost in breast carcinomas, this is likely due to hypermethylation during the early stages of neoplastic transformation (see Umbricht CB, Evron E, Gabrielson E, Ferguson A, Marks J, Sukumar S. Hypermethylation of 14-3-3 sigma (stratifin) is an early event in breast cancer. *Oncogene*. 2001 Jun 7;20(26):3348-53).

The gene PSA (Accession number NM_021154), also known as PSA-T, is not to be confused with the gene also popularly referred to as PSA (Accession number NM_001648) which encodes prostate specific antigen and whose technically correct name is kallikrein 3. The gene PSA-T encodes the protein phosphoserine aminotransferase which is the second step-catalysing enzyme in the serine biosynthesis pathway. Changes in gene expression levels have been monitored by mRNA expression analysis and upregulation of the gene has been identified in colonic carcinoma in a study of 6 samples (Ojala P, Sundstrom J, Gronroos JM, Virtanen E, Talvinen K, Nevalainen TJ. mRNA differential display of gene expression in colonic carcinoma. *Electrophoresis*. 2002; 23(11):1667-76).

The gene stathmin (NM_005563) codes for an oncoprotein 18, also known as stathmin, a conserved cytosolic phosphoprotein that regulates microtubule dynamics. The protein is highly expressed in a variety of human malignancies. In human breast cancers the stathmin gene has shown to be up-regulated in a subset of the tumours. The gene PRKCD encodes a member of the family of protein kinase c enzymes, and is involved in B cell signalling and in the regulation of growth, apoptosis, and differentiation of a variety of cell types.

Some of these molecules interact in a cascade-like manner. PRKCD activity that targets STMN1 is modulated by SFN binding and SYK phosphorylation. Together this influences tubulin polymerisation that is required for cell division.

Description

The present invention provides methods and nucleic acids for predicting the response of a patient with a cell proliferative disorder of the breast tissues to endocrine treatment. Using the methods and nucleic acids described herein, statistically significant models of patient responsiveness to said treatment regimen can be developed and utilised to assist patients and clinicians in determining treatment options. The described method is to be used to assess the suitability of endocrine treatment as a therapy for patients suffering from a cell proliferative disorder of the breast tissues. Thus, the present invention will be seen to reduce the problems associated with present treatment response prediction methods.

Using the methods and nucleic acids as described herein, patient responsiveness can be evaluated before or during endocrine treatment for a cell proliferative disorder of the breast tissues, in order to provide critical information to the patient and clinician as to the risks, burdens, and benefits associated endocrine treatment. It will be appreciated, therefore, that the methods and nucleic acids exemplified herein can serve to improve a patient's quality of life and odds of treatment success by allowing both patient and clinician a more accurate assessment of the patient's treatment options.

The aim of the invention is achieved by means of the analysis of the methylation patterns of one or a combination of genes taken from the group PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFBR2, COX7A2L (see Table 1) and/or their regulatory regions. The invention is characterised in that the nucleic acid of one or a combination of genes taken from the group PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFBR2 and COX7A2L are contacted with a reagent or series of reagents capable of distinguishing between methylated and non methylated CpG dinucleotides within the genomic sequence of interest.

The present invention makes available a method for ascertaining genetic and/or epigenetic parameters of genomic DNA. The method is for use in the improved treatment and monitoring of breast cell proliferative disorders, by enabling the accurate prediction of a patient's response to endocrine treatment. In a particularly preferred embodiment, the method according to the invention enables the differentiation between patients who respond to endocrine therapy and those who do not.

The method according to the invention may be used for the analysis of a wide variety of cell proliferative disorders of the breast tissues including, but not limited to ductal carcinoma *in situ*, lobular carcinoma, colloid carcinoma, tubular carcinoma, medullary carcinoma, metaplastic carcinoma, intraductal carcinoma *in situ*, lobular carcinoma *in situ* and papillary carcinoma *in situ*.

The method according to the invention is particularly suited to the prediction of response to endocrine treatment in two treatment settings. In one embodiment, the method is applied to patients who receive endocrine treatment as secondary treatment to a primary treatment such as surgery (hereinafter referred to as the adjuvant setting) as illustrated in Figure 1. Such a treatment is often prescribed to patients suffering from Stage 1 to 3 breast carcinomas. In this embodiment responders are defined as those who do not have a detectable relapse of the breast cancer in a specified period of time, non responders are those who relapse within said time period.

In a further preferred embodiment said method is applied to patients suffering from a relapse of breast cancer following treatment by a primary means (preferably surgery) followed by a disease free period, and wherein the endocrine treatment has been prescribed in response to a detection of a relapse of the carcinoma. Such a treatment is often prescribed to patients suffering from later stage carcinomas, particularly wherein metastasis has occurred. Therefore this clinical setting shall also hereinafter be referred to as the 'metastatic setting'. In this embodiment responders are those who enter partial or complete remission i.e. subjects whose cancer recedes to undetectable levels as opposed to those whose diseases further metastasise or remain above detectable levels. This methodology present further improvements over the state of the art in that the method may be applied to any subject, independent of the estrogen and/or progesterone receptor status. Therefore in a preferred embodiment, the subject is not required to have been tested for estrogen or progesterone receptor status.

Furthermore, the method enables the analysis of cytosine methylations and single nucleotide polymorphisms within said genes.

5 The object of the invention is achieved by means of the analysis of the methylation patterns of the genes PSA; STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFBR2 and COX7A2L and/or their regulatory regions, in a particularly preferred embodiment, the sequences comprising SEQ ID NOs: 27, 90, 41, 40, 121, 78, 115, 86, 43 and 105 and sequences complementary thereto. In a preferred embodiment said method is achieved by
10 contacting said nucleic acid sequences in a biological sample obtained from a subject with at least one reagent or a series of reagents, wherein said reagent or series of reagents, distinguishes between methylated and non methylated CpG dinucleotides within the target nucleic acid.

15 In a preferred embodiment, the method comprises the following steps:

In the first step of the method the genomic DNA sample must be isolated from sources such as cells or cellular components which contain DNA, sources of DNA comprising, for example, cell lines, histological slides, biopsies, tissue embedded in paraffin, breast tissues, blood, plasma, lymphatic fluid, lymphatic tissue, duct cells, ductal lavage fluid, nipple
20 aspiration fluid, bone marrow and combinations thereof. Extraction may be by means that are standard to one skilled in the art, these include the use of detergent lysates, sonification and vortexing with glass beads. Once the nucleic acids have been extracted the genomic double stranded DNA is used in the analysis.

25 In a preferred embodiment the DNA may be cleaved prior to the next step of the method, this may be by any means standard in the state of the art, in particular, but not limited to, with restriction endonucleases.

In the second step of the method, the genomic DNA sample is treated in such a manner that
30 cytosine bases which are unmethylated at the 5'-position are converted to uracil, thymine, or another base which is dissimilar to cytosine in terms of hybridisation behaviour. This will be understood as 'pretreatment' hereinafter.

The above described treatment of genomic DNA is preferably carried out with bisulfite (sulfite, disulfite) and subsequent alkaline hydrolysis which results in a conversion of non-methylated cytosine nucleobases to uracil or to another base which is dissimilar to cytosine in terms of base pairing behaviour. If bisulfite solution is used for the reaction, then an addition
5 takes place at the non-methylated cytosine bases. Moreover, a denaturing reagent or solvent as well as a radical interceptor must be present. A subsequent alkaline hydrolysis then gives rise to the conversion of non-methylated cytosine nucleobases to uracil. The converted DNA is then used for the detection of methylated cytosines.

10 Fragments of the pretreated DNA are amplified, using sets of primer oligonucleotides, and a preferably heat-stable, polymerase. Because of statistical and practical considerations, preferably more than six different fragments having a length of 100 - 2000 base pairs are amplified. The amplification of several DNA segments can be carried out simultaneously in one and the same reaction vessel. Usually, the amplification is carried out by means of a
15 polymerase chain reaction (PCR).

The design of such primers is obvious to one skilled in the art. These should include at least two oligonucleotides whose sequences are each reverse complementary or identical to an at least 18 base-pair long segment of the following base sequences specified in the appendix:
20 SEQ ID NO.188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586 and 587. Said primer oligonucleotides are preferably characterised in that they do not contain any CpG dinucleotides. In a particularly preferred embodiment of the method, the sequence of said
25 primer oligonucleotides are designed so as to selectively anneal to and amplify, only the breast cell specific DNA of interest, thereby minimising the amplification of background or non relevant DNA. In the context of the present invention, background DNA is taken to mean genomic DNA which does not have a relevant tissue specific methylation pattern, in this case, the relevant tissue being breast tissues.

30 According to the present invention, it is preferred that at least one primer oligonucleotide is bound to a solid phase during amplification. The different oligonucleotide and/or PNA-oligomer sequences can be arranged on a plane solid phase in the form of a rectangular or hexagonal lattice, the solid-phase surface preferably being composed of silicon, glass,

polystyrene, aluminium, steel, iron, copper, nickel, silver, or gold, it being possible for other materials such as nitrocellulose or plastics to be used as well.

The fragments obtained by means of the amplification may carry a directly or indirectly detectable label. Preferred are labels in the form of fluorescence labels, radionuclides, or detachable molecule fragments having a typical mass which can be detected in a mass spectrometer, it being preferred that the fragments that are produced have a single positive or negative net charge for better detectability in the mass spectrometer. The detection may be carried out and visualised by means of matrix assisted laser desorption/ionisation mass spectrometry (MALDI) or using electron spray mass spectrometry (ESD).

In the next step the nucleic acid amplicates are analysed in order to determine the methylation status of the genomic DNA prior to treatment.

The post treatment analysis of the nucleic acids may be carried out using alternative methods. Several methods for the methylation status specific analysis of the treated nucleic acids are described below, other alternative methods will be obvious to one skilled in the art.

Using several methods known in the art the analysis may be carried out during the amplification step of the method. In one such embodiment, the methylation status of preselected CpG positions within the genes PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFB2, COX7A2L PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFB2 and COX7A2L and/or their regulatory regions may be detected by use of methylation specific primer oligonucleotides. This technique has been described in U.S. Patent 6,265,171 to Herman. The use of methylation status specific primers for the amplification of bisulphite treated DNA allows the differentiation between methylated and unmethylated nucleic acids. MSP primers pairs contain at least one primer which hybridises to a bisulphite treated CpG dinucleotide. Therefore the sequence of said primers comprises at least one CG, TG or CA dinucleotide. MSP primers specific for non methylated DNA contain a 'T' at the 3' position of the C position in the CpG. According to the present invention, it is therefore preferred that the base sequence of said primers is required to comprise a sequence having a length of at least 9 nucleotides which hybridises to a pretreated nucleic acid sequence according to SEQ ID NOs.: 188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463,

344, 345, 586 and 587 and sequences complementary thereto wherein the base sequence of said oligomers comprises at least one CG, TG or CA dinucleotide.

In one embodiment of the method the methylation status of the CpG positions may be determined by means of hybridisation analysis. In this embodiment of the method the amplificates obtained in the second step of the method are hybridised to an array or a set of oligonucleotides and/or PNA probes. In this context, the hybridisation takes place in the manner described as follows. The set of probes used during the hybridisation is preferably composed of at least 4 oligonucleotides or PNA-oligomers. In the process, the amplificates serve as probes which hybridise to oligonucleotides previously bonded to a solid phase. The non-hybridised fragments are subsequently removed. Said oligonucleotides contain at least one base sequence having a length of 10 nucleotides which is reverse complementary or identical to a segment of the base sequences specified in the appendix, the segment containing at least one CpG or TpG dinucleotide. In a further preferred embodiment the cytosine of the CpG dinucleotide, or in the case of TpG, the thiamine, is the 5th to 9th nucleotide from the 5'-end of the 10-mer. One oligonucleotide exists for each CpG or TpG dinucleotide.

The non-hybridised amplificates are then removed. In the final step of the method, the hybridised amplificates are detected. In this context, it is preferred that labels attached to the amplificates are identifiable at each position of the solid phase at which an oligonucleotide sequence is located.

In a further embodiment of the method the methylation status of the CpG positions may be determined by means of oligonucleotide probes that are hybridised to the treated DNA concurrently with the PCR amplification primers (wherein said primers may either be methylation specific or standard).

A particularly preferred embodiment of this method is the use of fluorescence-based Real Time Quantitative PCR (Heid et al., Genome Res. 6:986-994, 1996) employing a dual-labelled fluorescent oligonucleotide probe (TaqManTM PCR, using an ABI Prism 7700 Sequence Detection System, Perkin Elmer Applied Biosystems, Foster City, California). The TaqManTM PCR reaction employs the use of a nonextendible interrogating oligonucleotide, called a TaqManTM probe, which is designed to hybridise to a GpC-rich sequence located between the forward and reverse amplification primers. The TaqManTM probe further

comprises a fluorescent "reporter moiety" and a "quencher moiety" covalently bound to linker moieties (e.g., phosphoramidites) attached to the nucleotides of the TaqMan™ oligonucleotide. For analysis of methylation within nucleic acids subsequent to bisulphite treatment it is required that the probe be methylation specific, as described in U.S. 6,331,393, (hereby incorporated by reference) also known as the Methyl Light assay. Variations on the TaqMan™ detection methodology that are also suitable for use with the described invention include the use of dual probe technology (Lightcycler™) or fluorescent amplification primers (Sunrise™ technology). Both these techniques may be adapted in a manner suitable for use with bisulphite treated DNA, and moreover for methylation analysis within CpG dinucleotides.

A further suitable method for the use of probe oligonucleotides for the assessment of methylation by analysis of bisulphite treated nucleic acids is the use of blocker oligonucleotides. The use of such oligonucleotides has been described in BioTechniques 23(4), 1997, 714-720 D. Yu, M. Mukai, Q. Liu, C. Steinman. Blocking probe oligonucleotides are hybridised to the bisulphite treated nucleic acid concurrently with the PCR primers. PCR amplification of the nucleic acid is terminated at the 5' position of the blocking probe, thereby amplification of a nucleic acid is suppressed wherein the complementary sequence to the blocking probe is present. The probes may be designed to hybridise to the bisulphite treated nucleic acid in a methylation status specific manner. For example, for detection of methylated nucleic acids within a population of unmethylated nucleic acids suppression of the amplification of nucleic acids which are unmethylated at the position in question would be carried out by the use of blocking probes comprising a 'CG' at the position in question, as opposed to a 'CA'.

In a further preferred embodiment of the method the determination of the methylation status of the CpG positions is carried out by the use of template directed oligonucleotide extension, such as MS SNUPE as described by Gonzalgo and Jones (Nucleic Acids Res. 25:2529-2531).

In a further embodiment of the method the determination of the methylation status of the CpG positions is enabled by sequencing and subsequent sequence analysis of the amplicate generated in the second step of the method (Sanger F., et al., 1977 PNAS USA 74: 5463-5467).

A further embodiment of the invention is a method for the analysis of the methylation status of genomic DNA without the need for pretreatment. In the first and second steps of the method the genomic DNA sample must be obtained and isolated from tissue or cellular sources. Such sources may include cell lines, histological slides, body fluids, or tissue
5 embedded in paraffin. Extraction may be by means that are standard to one skilled in the art, these include the use of detergent lysates, sonification and vortexing with glass beads. Once the nucleic acids have been extracted the genomic double stranded DNA is used in the analysis.

10 In a preferred embodiment the DNA may be cleaved prior to the treatment, this may be by any means standard in the state of the art, in particular with restriction endonucleases. In the third step, the DNA is then digested with one or more methylation sensitive restriction enzymes. The digestion is carried out such that hydrolysis of the DNA at the restriction site is informative of the methylation status of a specific CpG dinucleotide.

15 In a preferred embodiment the restriction fragments are amplified. In a further preferred embodiment this is carried out using the polymerase chain reaction.

20 In the final step the amplicates are detected. The detection may be by any means standard in the art, for example, but not limited to, gel electrophoresis analysis, hybridisation analysis, incorporation of detectable tags within the PCR products, DNA array analysis, MALDI or ESI analysis.

25 The aforementioned method is preferably used for ascertaining genetic and/or epigenetic parameters of genomic DNA.

In order to enable this method, the invention further provides the modified DNA of one or a combination of genes taken from the group PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFBR2, COX7A2L, PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN,
30 GRIN2D, TGFBR2 and COX7A2L as well as oligonucleotides and/or PNA-oligomers for detecting cytosine methylations within said genes. The present invention is based on the discovery that genetic and epigenetic parameters and, in particular, the cytosine methylation patterns of said genomic DNAs are particularly suitable for improved treatment and monitoring of breast cell proliferative disorders.

The nucleic acids according to the present invention can be used for the analysis of genetic and/or epigenetic parameters of genomic DNA.

This objective according to the present invention is achieved using a nucleic acid containing a sequence of at least 18 bases in length of the pretreated genomic DNA according to one of SEQ ID NOs: 188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586, 587, 188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586 and 587 and sequences complementary thereto.

The modified nucleic acids could heretofore not be connected with the ascertainment of disease relevant genetic and epigenetic parameters.

The object of the present invention is further achieved by an oligonucleotide or oligomer for the analysis of pretreated DNA, for detecting the genomic cytosine methylation state, said oligonucleotide containing at least one base sequence having a length of at least 10 nucleotides which hybridises to a pretreated genomic DNA according to SEQ ID NOs: 188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586 and 587. The oligomer probes according to the present invention constitute important and effective tools which, for the first time, make it possible to ascertain specific genetic and epigenetic parameters during the analysis of biological samples for features associated with a patient's response to endocrine treatment. Said oligonucleotides allow the improved treatment and monitoring of breast cell proliferative disorders. The base sequence of the oligomers preferably contains at least one CpG or TpG dinucleotide. The probes may also exist in the form of a PNA (peptide nucleic acid) which has particularly preferred pairing properties. Particularly preferred are oligonucleotides according to the present invention in which the cytosine of the CpG dinucleotide is within the middle third of said oligonucleotide e.g. the 5th - 9th nucleotide from the 5'-end of a 13-mer oligonucleotide; or in the case of PNA-oligomers, it is preferred for the cytosine of the CpG dinucleotide to be the 4th - 6th nucleotide from the 5'-end of the 9-mer.

The oligomers according to the present invention are normally used in so called "sets" which contain at least one oligomer for each of the CpG dinucleotides within SEQ ID NOs: 188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586 and 587.

In a particularly preferred embodiment of the method the oligomers according to SEQ ID NOs: 1816-1833, 1114-1129, 1808-1815, 1762-1769, 1552-1559, 1490-1499, 1138-1147 and 1686-1693 are used for predicting a subject's response to endocrine treatment in an metastatic setting.

In the case of the sets of oligonucleotides according to the present invention, it is preferred that at least one oligonucleotide is bound to a solid phase. It is further preferred that all the oligonucleotides of one set are bound to a solid phase.

The present invention further relates to a set of at least 10 n (oligonucleotides and/or PNA-oligomers) used for detecting the cytosine methylation state of genomic DNA, by analysis of said sequence or treated versions of said sequence (of the genes PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFBR2 and COX7A2L, as detailed in the sequence listing and Table 1) and sequences complementary thereto). These probes enable improved treatment and monitoring of breast cell proliferative disorders.

The set of oligomers may also be used for detecting single nucleotide polymorphisms (SNPs) by analysis of said sequence or treated versions of said sequence (of the genes PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFBR2 and COX7A2L, as detailed in the sequence listing and Table 1).

It will be obvious to one skilled in the art that the method according to the invention will be improved and supplemented by the incorporation of markers and clinical indicators known in the state of the art and currently used as predictive of the outcome Endocrine treatment. More preferably said markers include node status, age, menopausal status, grade, estrogen and progesterone receptors.

The genes that form the basis of the present invention may also be used to form a "gene panel", i.e. a collection comprising the particular genetic sequences of the present invention

and/or their respective informative methylation sites. The formation of gene panels allows for a quick and specific analysis of specific aspects of breast cancer treatment. The gene panel(s) as described and employed in this invention can be used with surprisingly high efficiency for the treatment of breast cell proliferative disorders by prediction of the outcome of treatment with a therapy comprising one or more drugs which target the estrogen receptor pathway or are involved in estrogen metabolism, production, or secretion.

The efficiency of the method according to the invention is improved when applied to patients who have not been treated with chemotherapy. Accordingly, it is a particularly preferred embodiment of the method wherein the method is used for the assessment of subjects who have not undergone chemotherapy.

In addition, the use of multiple CpG sites from a diverse array of genes allows for a relatively high degree of sensitivity and specificity in comparison to single gene prognostic tools.

According to the present invention, it is preferred that an arrangement of different oligonucleotides and/or PNA-oligomers (a so-called "array") made available by the present invention is present in a manner that it is likewise bound to a solid phase. This array of different oligonucleotide- and/or PNA-oligomer sequences can be characterised in that it is arranged on the solid phase in the form of a rectangular or hexagonal lattice. The solid phase surface is preferably composed of silicon, glass, polystyrene, aluminium, steel, iron, copper, nickel, silver, or gold. However, nitrocellulose as well as plastics such as nylon which can exist in the form of pellets or also as resin matrices are suitable alternatives.

Therefore, a further subject matter of the present invention is a method for manufacturing an array fixed to a carrier material for the improved treatment and monitoring of breast cell proliferative disorders. In said method at least one oligomer according to the present invention is coupled to a solid phase. Methods for manufacturing such arrays are known, for example, from US Patent 5,744,305 by means of solid-phase chemistry and photolabile protecting groups.

A further subject matter of the present invention relates to a DNA chip for the improved treatment and monitoring of breast cell proliferative disorders. The DNA chip contains at least

one nucleic acid according to the present invention. DNA chips are known, for example, in US Patent 5,837,832.

Moreover, a subject matter of the present invention is a kit which may be composed, for example, of a bisulfite-containing reagent, a set of primer oligonucleotides containing at least two oligonucleotides whose sequences in each case correspond to or are complementary to a 18 base long segment of the base sequences specified in SEQ ID NOs: 188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586 and 587 and/or PNA-oligomers as well as instructions for carrying out and evaluating the described method.

In a further preferred embodiment said kit may further comprise standard reagents for performing a CpG position specific methylation analysis wherein said analysis comprises one or more of the following techniques: MS-SNuPE, MSP, Methyl light, Heavy Methyl, and nucleic acid sequencing. However, a kit along the lines of the present invention can also contain only part of the aforementioned components.

The oligomers according to the present invention or arrays thereof as well as a kit according to the present invention are intended to be used for the improved treatment and monitoring of breast cell proliferative disorders. According to the present invention, the method is preferably used for the analysis of important genetic and/or epigenetic parameters within genomic DNA, in particular for use in improved treatment and monitoring of breast cell proliferative disorders.

The methods according to the present invention are used, for improved treatment and monitoring of breast cell proliferative disorder by enabling more informed treatment regimens.

The present invention moreover relates to the diagnosis and/or prognosis of events which are disadvantageous or relevant to patients or individuals in which important genetic and/or epigenetic parameters within genomic DNA, said parameters obtained by means of the present invention may be compared to another set of genetic and/or epigenetic parameters, the differences serving as the basis for the diagnosis and/or prognosis of events which are

disadvantageous or relevant to patients or individuals. Examples of such parameters include, but are not limited to the assessment of estrogen and progesterone markers.

5 In the context of the present invention the term "hybridisation" is to be understood as a bond of an oligonucleotide to a completely complementary sequence along the lines of the Watson-Crick base pairings in the sample DNA, forming a duplex structure.

10 In the context of the present invention, "genetic parameters" are mutations and polymorphisms of genomic DNA and sequences further required for their regulation. To be designated as mutations are, in particular, insertions, deletions, point mutations, inversions, and polymorphisms and, particularly preferred, SNPs (single nucleotide polymorphisms).

15 In the context of the present invention the term "methylation state" is taken to mean the degree of methylation present in a nucleic acid of interest, this may be expressed in absolute or relative terms i.e. as a percentage or other numerical value or by comparison to another tissue and therein described as hypermethylated, hypomethylated or as having significantly similar or identical methylation status.

20 In the context of the present invention the term "regulatory region" of a gene is taken to mean nucleotide sequences which affect the expression of a gene. Said regulatory regions may be located within, proximal or distal to said gene. Said regulatory regions include but are not limited to constitutive promoters, tissue-specific promoters, developmental-specific promoters, inducible promoters and the like. Promoter regulatory elements may also include certain enhancer sequence elements that control transcriptional or translational efficiency of the gene.

25 In the context of the present invention the term "chemotherapy" is taken to mean the use of drugs or chemical substances to treat cancer. This definition excludes radiation therapy (treatment with high energy rays or particles), hormone therapy (treatment with hormones or hormone analogues (synthetic substitutes) and surgical treatment.

30 In the context of the present invention, "epigenetic parameters" are, in particular, cytosine methylations and further modifications of DNA bases of genomic DNA and sequences further required for their regulation. Further epigenetic parameters include, for example, the

acetylation of histones which, cannot be directly analysed using the described method but which, in turn, correlates with the DNA methylation.

In the context of the present invention the term "adjuvant treatment" is taken to mean a therapy of a cancer patient immediately following an initial non chemotherapeutical therapy, e.g. surgery. In the context of the present invention, said adjuvant treatment is performed using Tamoxifen. In general, the purpose of an adjuvant therapy is to provide a significantly smaller risk of recurrences compared without the adjuvant therapy.

In the context of the present invention the term "estrogen and/or progesterone receptor positive" is taken to mean cells that expresses on its surface receptors that are susceptible to the binding of estrogens and/or progesterones.

In the following, the present invention will be explained in greater detail on the basis of the sequences, figures and examples without being limited thereto.

Figure 1 shows a preferred application of the method according to the invention. The X axis shows the tumour(s) mass, wherein the line '3' shows the limit of detectability. The Y-axis shows time. Accordingly said figure illustrates a simplified model of endocrine treatment of an Stage 1-3 breast tumour wherein primary treatment was surgery (at point 1), followed by adjuvant therapy with Tamoxifen. In a first scenario a responder to treatment (4) is shown as remaining below the limit of detectability for the duration of the observation. A non responder to the treatment (5) has a period of disease free survival (2) followed by relapse when the carcinoma mass reaches the level of detectability.

Figure 2 shows another preferred application of the method according to the invention. The X axis shows the tumour(s) mass, wherein the line '3' shows the limit of detectability. The Y-axis shows time. Accordingly said figure illustrates a simplified model of Endocrine treatment of an late stage breast tumour wherein primary treatment was surgery (at point 1), followed by relapse which is treated by Tamoxifen (2). In a first scenario a responder to treatment (4) is shown as remaining below the limit of detectability for the duration of the observation. A non responder to the treatment (5) does not recover from the relapse.

Figure 3 shows the methylation analysis of CpG islands according to Example 1. CpG islands per gene were grouped and their correlation with objective response determined by Hotelling's T^2 statistics. Black dots indicate the P -value of the indicated gene. The 20 most informative genes, ranked from left to right with increasing P -value, are shown. The top dotted line marks the uncorrected significance value ($P < 0.05$). The lower dotted line marks significance after false discovery rate correction of 25%. All genes with a P -value smaller or equal to the gene with the largest P -value that is below the lower line (in this case COX7A2L) are considered significant. The FDR correction chosen guarantees that the identified genes are with 75% chance true discoveries.

Figure 4 shows the raw CpG dinucleotide methylation data of the 10 genes that significantly correlated with the overall response rate as determined in Figure 3 (Example 1). Tumours from objective responders (CR + PR) are shown on the left; tumours from patients with progressive disease (PD) are shown on the right. The shades of grey represent the relative distance of the CpG dinucleotide methylation status from the mean value. CpG dinucleotides are grouped per gene. The indicated genes are ordered from top to bottom with increasing significance. Light grey represents a hypomethylated CpG dinucleotide while darker grey indicates a hypermethylated CpG dinucleotide. Methylation data are centered and normalised to one standard deviation for every individual CpG dinucleotide.

Figure 5 shows the progression-free survival (PFS) curves of combination scores according to Example 1. PFS curves after start of tamoxifen treatment of patients are shown. They are grouped using a predictive score ($\chi^2=14.0$; 3 degrees of freedom) based on the traditional predictive markers age, dominant site of relapse, disease-free interval and ER level (A). A DNA methylation-based score ($\chi^2=27.5$; 3 degrees of freedom) is presented comprising the statistically independent predicting genes phosphoserine amino transferase (PSA-T), stathmin (STMN1), S100 protein A2 (S100A2), transforming growth factor β receptor II (TGFB2), and glutamate receptor 2D (GRIN2D) (B). Survival curves were generated and significance calculated as described in Example 1. The calculated predictive scores were divided into 4 groups (q1 – q4) with 50 patients each and using the 25th, 50th, and 75th percentile of the values. The numbers below the X-axis represent the number of patients at risk in each group at the indicated time points of 0, 12, 24, and 36 months. Progression free survival (in percentage) is plotted on the Y-axis and time to progression (in months) is plotted on the X-axis.

SEQ ID NOs: 1 to 121 represent 5' and/or regulatory regions and/or CpG rich regions of the genes according to Table 1. These sequences are derived from Genbank and will be taken to include all minor variations of the sequence material which are currently unforeseen, for example, but not limited to, minor deletions and SNPs.

SEQ ID NOs: 136 to 619 exhibit the pretreated sequence of DNA derived from the genomic sequence according to Table 1. These sequences will be taken to include all minor variations of the sequence material which are currently unforeseen, for example, but not limited to, minor deletions and SNPs.

SEQ ID NO: 856 to SEQ ID NO: 1843 exhibit the sequence of oligomers which are particularly useful for the analysis of pretreated DNA according to SEQ ID NO: 136 to SEQ ID NO: 619.

Examples

In the following example, candidate genes were analysed by means of high throughput methylation analysis methods. A set of 200 breast cancer samples from advanced breast cancer patients, treated with the anti-estrogen drug tamoxifen were analyzed. The measurable effect of endocrine therapy on the size of the metastatic lesion, and on progression free survival time (PFS) was used as the main clinical endpoints of the study. In total, 499 CpGs in the promoter regions of 117 genes (2 to 6 CpGs per gene) were analyzed.

Example 1

In the first step the genomic DNA was isolated from the cell samples using the Wizzard kit (Proméga).

The isolated genomic DNA from the samples were treated using a bisulfite solution (hydrogen sulfite, disulfite). The treatment was such that all non methylated cytosines within the sample were converted to thiamidine, conversely 5-methylated cytosines within the sample remain unmodified.

The treated nucleic acids were then amplified using multiplex PCRs, amplifying 8 fragments per reaction with Cy5 fluorescently labelled primers. PCR primers used are described in Table 2. PCR conditions were as follows.

5 Reaction solution:

10 ng bisulfite treated DNA

3,5 mmol/l $MgCl_2$

400 μ mol/l dNTPs

2 pmol each primer

10 1 U Hot Star Taq (Qiagen)

Forty cycles were carried out as follows. Denaturation at 95°C for 15 min, followed by annealing at 55°C for 45 sec, primer elongation at 65°C for 2 min. A final elongation at 65°C was carried out for 10 min.

15

All PCR products from each individual sample were then hybridised to glass slides carrying a pair of immobilised oligonucleotides for each CpG position under analysis. Each of these detection oligonucleotides was designed to hybridise to the bisulphite converted sequence around one CpG site which was either originally unmethylated (TG) or methylated (CG). See Table 2 for further details of all hybridisation oligonucleotides used. Hybridisation conditions were selected to allow the detection of the single nucleotide differences between the TG and CG variants.

20

5 μ l volume of each multiplex PCR product was diluted in 10 x Ssarc buffer (10 x Ssarc: 230 ml 20 x SSC, 180 ml sodium lauroyl sarcosinate solution 20%, dilute to 1000 ml with dH₂O).

25

The reaction mixture was then hybridised to the detection oligonucleotides as follows. Denaturation at 95°C, cooling down to 10°C, hybridisation at 42°C overnight followed by washing with 10 x Ssarc and dH₂O at 42°C.

30

Fluorescent signals from each hybridised oligonucleotide were detected using genepix scanner and software. Ratios for the two signals (from the CG oligonucleotide and the TG oligonucleotide used to analyse each CpG position) were calculated based on comparison of intensity of the fluorescent signals.

Data analysis

In order to determine the ability of each gene promoter to predict success or failure of Tamoxifen treatment, the individual CpGs measured were combined per gene using Hotelling's T^2 statistics. To identify potential markers, we performed our initial analysis on those 123 patients who showed the extreme types of response; either an objective response (CR+PR, 45 patients) or a progressive disease right from the start of treatment (PD, 78 patients). Ten genes were significantly associated with a response to tamoxifen after correcting for multiple comparison with a moderate conservative false discovery rate of 25% (see Figure 3). The genes were PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFBR2 and COX7A2L. Furthermore, from the DNA methylation data matrix (Figure 4), we concluded that for the majority of the genes CpG island hypermethylation was correlated with favourable response to tamoxifen treatment, while for stathmin 1/ oncoprotein 18 (STMN1) and stratifin/14-3-3 protein σ (SFN) hypomethylation was associated with remission.

Subsequently, all 200 patients including those with an intermediate type of response (59 patients with stable disease (SD, no change of disease for more than 6 months) and 18 patients with stable disease for 6 months or less) were analysed in logistic regression analysis. For each of the 10 selected genes, we combined per gene the estimates from the logistic regression for overall response (= objective response + SD) of the different CpG dinucleotides measured. In the whole cohort, for all ten genes, the response rate to tamoxifen treatment was approximately 15 to 20% higher (odd ratios [OR's] ranging from 1.5 to 3.5) for patients whose tumours had a favourable DNA methylation status than those with an unfavourable status. In concordance, for the 10 genes, the median PFS in the former group of patients was on average 1.8 times longer than that in the latter group (hazard ratios (HR's) ranging from 0.54 to 0.77). Thus, also in the complete cohort, these 10 genes were associated with disease outcome after tamoxifen treatment.

Prediction of response to tamoxifen treatment in advanced breast cancer patients is based traditionally on the patient, disease, and tumour characteristics (Pyrhonen S, Ellmen J, Vuorinen J, Gershanovich M, Tominaga T, Kaufmann M, Hayes DF. Meta-analysis of trials comparing toremifene with tamoxifen and factors predicting outcome of antiestrogen therapy in postmenopausal women with breast cancer. *Breast Cancer Res Treat.* 1999 ;56(2):133-43), i.e., age, first dominant site of relapse, disease-free interval, and ER status. We compared a predictive score calculated with the multivariable estimates of the traditional predictive

factors (traditional factors-based score) with a score derived from DNA methylation data only (DNA methylation-based score). For a DNA methylation-based score, we included only genes whose DNA methylation status predicted response independent of each other. To establish this, we added the DNA methylation status information of each of the 10 genes simultaneously to a multivariable logistic regression model. After backward elimination of the non-significant genes ($P < 0.05$), five genes, *i.e.* phosphoserine amino transferase (PSA-T), stathmin (STMN1), S100 protein A2 (S100A2), transforming growth factor β receptor II (TGFB2), and glutamate receptor 2D (GRIN2D), were statistically significant and predicted response, independent of one another. The DNA methylation-based score that was subsequently compared to the traditional factors-based score was derived from the multivariable estimates of these five genes.

The score for each tumour based on either traditional predictive factors or DNA methylation status was used to divide the patients into 4 groups by its 25th, 50th, and 75th percentile values (Table 3). The DNA methylation-based score showed a much better discriminatory strength with overall response than the traditional factors-based score (Table 3). The overall response rates in the DNA methylation-based score increased from 26% for the patients in the first quarter (q1) (OR set at 1.0), 34% for in the second quarter (q2) (OR=1.5), 66% in third for q3 (OR=5.5) and 82% and last quarter for q4 (OR=13.0) ($P < 0.001$) while for the traditional factors-based score the rates increased only from 36% (OR, set at 1.0) for q1 of this score, via 46% (OR=1.5) (q2) to 64% (OR=3.2) and 62% (OR=2.9) (q3) (q4), respectively ($P = 0.013$) (Table 3).

Similarly, median PFS in the extreme quarters for the DNA methylation-based score differed 4.2 times (from 3.8 to 16.1 months) while for the traditional factors-based score the difference between the two extreme quarters was only half of that (2.1 times; from 4.7 to 9.7 months) (compare curves of Fig. 5A with Fig. 5B).

Hence, we have shown for the first time that an epigenetic profile based on the CpG island DNA methylation status of promoter regions of just five genes can predict the likelihood of therapy response in patients with ER-positive advanced breast cancer treated with tamoxifen therapy. Furthermore, it appeared that this prediction was much more accurate than the prediction based on commonly used traditional predictive factors, suggesting that DNA methylation analysis may be useful for clinical therapy decisions. Epigenetic profiling of

tumour tissue DNA can therefore be a competitive and simple alternative for tedious mRNA profiling that is highly dependent on well-preserved tumour tissue material. Besides that epigenetic DNA profiles are very stable, are localised to specific sites (the promoter region of a gene) and can be easily amplified by PCR. Above and beyond, DNA methylation status determination can be performed on archived frozen or easily accessible paraffin-embedded tumour tissue material, making it widely applicable in the routine clinical setting.

Table 1: Genes amplified according to Example 1,

No:	Gene:	Primer:	Amplificate Length:
1	ABCB1 (SEQ ID NO: 1)	TAAGTATGTTGAAGAAAGATTATTGT AG (SEQ ID NO: 620) TAAAAACTATCCCATAATAACTCCCA AC (SEQ ID NO: 621)	633
2	APOC2 (SEQ ID NO: 2)	ATGAGTAGAAGAGGTGATAT (SEQ ID NO: 622) CCCTAAATCCCTTTCTTACC (SEQ ID NO: 623)	533
3	CACNA1G (SEQ ID NO: 3)	GGGATTTAAGAGAAATTGAGGTA (SEQ ID NO: 624) AAACCCCAAAACATCCTTTAT (SEQ ID NO: 625)	707
4	EGR4 (SEQ ID NO: 4)	AGGGGGATTGAGTGTTAAGT (SEQ ID NO: 627) CCCAAACATAAAACACAAAAT (SEQ ID NO: 626)	293
5	AR (SEQ ID NO: 5)	GTAGTAGTAGTAGTAAGAGA (SEQ ID NO: 628) ACCCCCTAAATAATTATCCT (SEQ ID NO: 629)	460
6	RB1 (SEQ ID NO: 6)	TTTAAGTTTGTITTTTGTITTTGGT (SEQ ID NO: 630) TCCTACTCTAAATCCTCCTCAA (SEQ ID NO: 631)	718
7	GP1BB (SEQ ID NO: 7)	GGTGATAGGAGAATAATGTTGG (SEQ ID NO: 632) TCTCCCAACTACAACCAAAC (SEQ ID NO: 633)	379

		NO: 633)	
8	WT1 (SEQ ID NO: 8)	AAAGGGGAAATTAAGTGTGT (SEQ ID NO: 635) TAACTACCCTCAACTTCCC (SEQ ID NO: 634)	747
9	HLA-F (SEQ ID NO: 9)	TTGTTGTTTTAGGGGTTTTGG (SEQ ID NO: 636) TCCTTCCCATTCTCCAAATATC (SEQ ID NO: 637)	946
10	ELK1 (SEQ ID NO: 10)	AAGTGTTTTAGTTTTAATGGGTA (SEQ ID NO: 638) CAAACCCAAAACCTACCTAT (SEQ ID NO: 639)	966
11	ARHI (SEQ ID NO: 12)	GTGAGTTTTTGGGGTGTTTA (SEQ ID NO: 640) TCAATCTTACTTTCACACTACATAA (SEQ ID NO: 641)	442
12	BCL2 (SEQ ID NO: 13)	GTATTTTATGTTAAGGGGGAAA (SEQ ID NO: 642) AAAAACCACAATCCTCCC (SEQ ID NO: 643)	640
13	BRCA1 (SEQ ID NO: 14)	TGGATGGGAATTGTAGTTTT (SEQ ID NO: 644) TTAACCACCCAATCTACCC (SEQ ID NO: 645)	537
14	CALCA (SEQ ID NO: 15)	GTTTTGGAAGTATGAGGGTG (SEQ ID NO: 646) CCAAATCTAAACCAATTTC (SEQ ID NO: 647)	614
15	CCND2 (SEQ ID NO: 16)	TTTTGGTATGTAGGTTGGATG (SEQ ID NO: 648) CCTAACCTCCTTCTTTAACT (SEQ ID NO: 649)	426
16	CDH1 (SEQ ID NO: 17)	GAGGTTGGGGTTAGAGGAT (SEQ ID NO: 650) CAAACTCACAAATACITTACAATTC (SEQ ID NO: 651)	478
17	CDKN1B (SEQ	GTGGGGAGGTAGTTGAAGA (SEQ ID	478

	ID NO: 18)	NO: 652) ATACACCCCTAACCCAAAAT (SEQ ID NO: 653)	
18	CDKN2A (SEQ ID NO: 19)	TTGAAAATTAAGGGTTGAGG (SEQ ID NO: 654) CACCCTCTAATAACCAACCA (SEQ ID NO: 655)	598
19	CDKN2A (SEQ ID NO: 19)	GGGGTTGGTTGGTTATTAGA (SEQ ID NO: 656) AACCTCTACCCACCTAAAT (SEQ ID NO: 657)	256
20	CDKN2B (SEQ ID NO: 20)	GGTTGGTTGAAGGAATAGAAAT (SEQ ID NO: 658) CCCCTAAACATACCCTTATTC (SEQ ID NO: 659)	708
21	CD44 (SEQ ID NO: 21)	GAAAGGAGAGGTTAAAGGTTG (SEQ ID NO: 660) AACTCACTTAACCTCAATCCC (SEQ ID NO: 661)	696
22	CSPG2 (SEQ ID NO: 22)	GGATAGGAGTTGGGATTAAGAT (SEQ ID NO: 662) AAATCTTTTCAACACCAAAAT (SEQ ID NO: 663)	414
23	DAPK1 (SEQ ID NO: 23)	AACCCTTTCTTCAAATTACAAA (SEQ ID NO: 664) TGATTGGGTTTTAGGAAATA (SEQ ID NO: 665)	348
24	GGT1 (SEQ ID NO: 24)	GTGAAGGGTGTGAGTTGTTTA (SEQ ID NO: 666) CACAATCAATTTCCACAA (SEQ ID NO: 667)	562
25	GSTP1 (SEQ ID NO: 25)	ATTGGGAAAGAGGGAAAG (SEQ ID NO: 668) TAAAAACTCTAAACCCCATCC (SEQ ID NO: 669)	300
26	HIC1 (SEQ ID NO: 26)	TGGGTTGGAGAAGAAGTTTA (SEQ ID NO: 670) TCATATTTCAAAAACACACC (SEQ ID	280

		NO: 671)	
27	STMN1 (SEQ ID NO: 27)	GAGTTTGTATTTAAGTTGAGTGGTT (SEQ ID NO: 672) AACAAAACAATACCCCTTCTAA (SEQ ID NO: 673)	334
28	STK11 (SEQ ID NO: 28)	TAAAAGAAGGATTTTGATTGG (SEQ ID NO: 675) CATCTTAATTACCTCCCTCCC (SEQ ID NO: 674)	528
29	ING4 (SEQ ID NO: 29)	ATTAGGGATGAGAGGATTTGTA (SEQ ID NO: 676) TCTTCCTAACCATACACACTAACC (SEQ ID NO: 677)	212
30	MGMT (SEQ ID NO: 30)	AAGGTTTTAGGGAAGAGTGTIT (SEQ ID NO: 678) ACCTTTTCCTATCACAAAATAA (SEQ ID NO: 679)	636
31	MLH1 (SEQ ID NO: 31)	TAAGGGGAGAGGAGGAGTTT (SEQ ID NO: 680) ACCAATTCTCAATCATCTCTTT (SEQ ID NO: 681)	545
32	MYC (SEQ ID NO: 33)	AGAGGGAGTAAAAGAAAATGGT (SEQ ID NO: 682) CCAAATAAACAAAATAACCTCC (SEQ ID NO: 683)	712
33	N33 (SEQ ID NO: 35)	TTTAGATTGAGGTTTtagggT (SEQ ID NO: 684) ATCCATTCTACCTCCTTTTCT (SEQ ID NO: 685)	497
34	PAX6 (SEQ ID NO: 36)	GGAGGGGAGAGGGTTATG (SEQ ID NO: 686) TACTATACACACCCCAAAACAA (SEQ ID NO: 687)	374
35	X51730 PGR	TTTGGAATGGGTTGTAT (SEQ ID	369

	(SEQ ID NO: 67)	NO: 746) CTACCCTTAACCTCCATCCTA (SEQ ID NO: 747)	
36	PTEN (SEQ ID NO: 38)	TTTTAGGTAGTTATATTGGGTATGTT (SEQ ID NO: 690) TCAACTCTCAAACCTCCATCA (SEQ ID NO: 691)	346
37	RARB (SEQ ID NO: 39)	TTGTTGGGAGTTTTAAAGTTTT (SEQ ID NO: 692) CAAATTCTCCTTCCAAATAAAT (SEQ ID NO: 693)	353
38	SFN (SEQ ID NO: 40)	GAAGAGAGGAGAGGGAGGTA (SEQ ID NO: 695) CTATCCAACAAACCCAACA (SEQ ID NO: 694)	489
39	S100A2 (SEQ ID NO: 41)	GTTTTTAAGTTGGAGAAGAGGA (SEQ ID NO: 696) ACCTATAAATCACAACCCACTC (SEQ ID NO: 697)	460
40	TGFBR2 (SEQ ID NO: 43)	GTAATTTGAAGAAAGTTGAGGG (SEQ ID NO: 698) CCAACAACATAACAAAACCTCT (SEQ ID NO: 699)	296
41	TIMP3 (SEQ ID NO: 44)	TGAGAAAATTGTTGTTTGAAGT (SEQ ID NO: 700) CAAAATACCCTAAAAACCACTC (SEQ ID NO: 701)	306
42	VHL (SEQ ID NO: 45)	TGTAATAATGAATAAAGTTAATGAGTG (SEQ ID NO: 702) TCCTAAATTCAAATAATCCTCCT (SEQ ID NO: 703)	362
43	CDKN1C (SEQ ID NO: 46)	GGGGAGGTAGATATTGGATAA (SEQ ID NO: 704) AACTACACCATTATATTCCCAC (SEQ ID NO: 705)	300

44	CAV1 (SEQ ID NO: 47)	GTTAGTATGTTTGGGGGTAAAT (SEQ ID NO: 707) ATAAATAACACCTTCCACCCTA (SEQ ID NO: 706)	435
45	CDH13 (SEQ ID NO: 48)	TTTGTATTAGGTGGAAGTGGT (SEQ ID NO: 708) CCCAAATAAATCAACAACAACA (SEQ ID NO: 709)	286
46	NDRG1 (SEQ ID NO: 49)	GGTTTGGGTTTAGTGGTAAAT (SEQ ID NO: 711) AACTTCATAACTCACCTTTC (SEQ ID NO: 710)	416
47	PTGS2 (SEQ ID NO: 50)	GATTTTGGAGAGGAAGTTAAG (SEQ ID NO: 713) AAAACATAAAACCAACCCATA (SEQ ID NO: 712)	381
48	THBS1 (SEQ ID NO: 51)	TGGGGTAGTTTAGGATAGG (SEQ ID NO: 714) CTTAAAAACACTAAAACTTCTCAAA (SEQ ID NO: 715)	398
49	TMEFF2 (SEQ ID NO: 52)	TTGTTTGGGTAAATAATGGA (SEQ ID NO: 716) CTTCTCTCTCTCCCCCTCTC (SEQ ID NO: 717)	295
50	PLAU (SEQ ID NO: 53)	TATTATAGGAGGATTGAGGAGG (SEQ ID NO: 718) CCCATAAAATCATACCACTTCT (SEQ ID NO: 719)	499
51	TMEFF2 (SEQ ID NO: 54)	TGTTGGTTGTTGTTGTTGTT (SEQ ID NO: 720) CTTCTACCCATCCCAAAA (SEQ ID NO: 721)	319
52	DNMT1 (SEQ ID NO: 55)	TCCCCATCACACCTAAAA (SEQ ID NO: 722) GGGAGGAGGGGATGTATT (SEQ ID NO: 723)	210
53	ESR1 (SEQ ID NO: 56)	AGGGGGAATTAAATAGAAAGAG (SEQ ID NO: 724)	662

	NO: 70)	ID NO: 752) CAATAAAACCATCCCAAATACT (SEQ ID NO: 753)	
54	APAF1 (SEQ ID NO: 57)	AGATATGTTTGGAGATTTAGGA (SEQ ID NO: 726) AACTCCCCACCTCTAATCTAT (SEQ ID NO: 727)	674
55	HOXA5 (SEQ ID NO: 58)	AAACCCCAAACAACCTCTAT (SEQ ID NO: 729) GAAGGGGGAAAGTTATTTAGTTA (SEQ ID NO: 728)	392
56	RASSF1 (SEQ ID NO: 59)	ACCTCTCTACAAATTACAAATTCA (SEQ ID NO: 730) AGTTTGGGTTAGTTTGGGTT (SEQ ID NO: 731)	347
57	BRCA2 (SEQ ID NO: 60)	AECACCCAAACCTAACT (SEQ ID NO: 733) GGTTGGTAGAGATAAAAGGGA (SEQ ID NO: 732)	388
58	CCND1 (SEQ ID NO: 61)	GATTATAGGGGAGTTTTGTTGA (SEQ ID NO: 734) CACCTCCAACATCCAAATA (SEQ ID NO: 735)	404
59	EDNRB (SEQ ID NO: 62)	TCAAAACATCCTCTATCTCTCC (SEQ ID NO: 737) ATAATTGGGGGTTGTATGTATT (SEQ ID NO: 736)	484
60	EGFR (SEQ ID NO: 63)	GGGTTTGGTTGTAATATGGATT (SEQ ID NO: 738) CCCAACACTACCCCTCTAA (SEQ ID NO: 739)	732
61	ERBB2 (SEQ ID NO: 64)	GAGGTAGAGGTTGTGGTGAGT (SEQ ID NO: 740) TCCCAACTTCACTTTCTCC (SEQ ID NO: 741)	528
62	FOS (SEQ ID	ATCTCCACTTCTACTTCCA (SEQ ID	500

	NO: 65)	NO: 743) TTTTAGGGTTATAGGGAAAGGT (SEQ ID NO: 742)	
63	NFKB1 (SEQ ID NO: 66)	TTTGTAGAATGAAAAGTAGAGTGTG (SEQ ID NO: 744) ACCTTAAAAACCCCAACAAT (SEQ ID NO: 745)	485
64	X51730 PGR (SEQ ID NO: 67)	TTTTGGGAATGGGTGTAT (SEQ ID NO: 746) CTACCCTTAACCTCCATCCTA (SEQ ID NO: 747)	369
65	TP53 (SEQ ID NO: 68)	GAGTAGGTAGTTGTTGGGTTTC (SEQ ID NO: 748) ACCCCTAATTTAACACTTCTCA (SEQ ID NO: 749)	702
66	TP73 (SEQ ID NO: 69)	AGTAAATAGTGGGTGAGTTATGAA (SEQ ID NO: 750) GAAAAACCTCTAAAACTACTCTCC (SEQ ID NO: 751)	607
67	ESR1 (SEQ ID NO: 70)	AGGGGGAATTAAATAGAAAGAG (SEQ ID NO: 752) CAATAAAACCATCCCAAATACT (SEQ ID NO: 753)	662
68	SERPINE1 (SEQ ID NO: 71)	GGGGTATAGAGAGAGTTGGAT (SEQ ID NO: 754) ACAATTAACAAACCCCAATAA (SEQ ID NO: 755)	492
69	CALM1 (SEQ ID NO: 72)	AAAACTCTAACCTTCTCAAA (SEQ ID NO: 757) TATTTTATAGTTGGGGTGTGT (SEQ ID NO: 756)	414
70	CSNK2B (SEQ ID NO: 73)	TACCCCTCACCATTACTCTAAC (SEQ ID NO: 759) TAGTTTGTGTTTATTGGGTGA (SEQ ID NO: 758)	437

71	FGFR1 (SEQ ID NO: 74)	AGGGAGTTAGTGGTGTGGTAT (SEQ ID NO: 760) CCTTTACCCTTCTCAAATCTAA (SEQ ID NO: 761)	367
72	MKI67 (SEQ ID NO: 75)	CCAATACTCTACAACCATCAAA (SEQ ID NO: 763) GGGAAGTTGAAGTAGGAAGAT (SEQ ID NO: 762)	499
73	NPM1 (SEQ ID NO: 76)	AAGGAAGGAGGAAGTAATTTGT (SEQ ID NO: 764) TTACACCAACCCTAAACTAAC (SEQ ID NO: 765)	454
74	MAPK1 (SEQ ID NO: 77)	TTTAGATAATTTAGGATGGGG (SEQ ID NO: 766) TTCTCATTACAAAAACAAAAA (SEQ ID NO: 767)	743
75	SYK (SEQ ID NO: 78)	GTGGGTTTTGGGTAGTTATAGA (SEQ ID NO: 768) TAACCTCCTCTCCTTACCAA (SEQ ID NO: 769)	485
76	TK2 (SEQ ID NO: 79)	ATACAACTCAAATCCTATCCA (SEQ ID NO: 771) AGGGAGAAGGAAGTTATTTGTT (SEQ ID NO: 770)	485
77	HSPB1 (SEQ ID NO: 80)	CCTACCTCTACCACTTCTCAAT (SEQ ID NO: 773) AAGAGGGTTTAGTTTATTTGG (SEQ ID NO: 772)	216
78	TES (SEQ ID NO: 81)	AGGTTGGGGATTTTAGTTTTT (SEQ ID NO: 774) ACCTTCTTCACTTTATTTTCCA (SEQ ID NO: 775)	448
79	SDC4 (SEQ ID NO: 82)	CCTAACTACCCTATTCTTTT (SEQ ID NO: 777)	269

		AGTTGGGGAAATTAAGGTTTAG (SEQ ID NO: 776)	
80	PITX2 (SEQ ID NO: 83)	TCCTCAACTCTACAAACCTAAAA (SEQ ID NO: 779) GTAGGGGAGGGAAGTAGATGT (SEQ ID NO: 778)	408
81	GPR37 (SEQ ID NO: 84)	ACTATTTTCTTTTCCTCTAAAAAC (SEQ ID NO: 781) TATGGTTTGGTGAGGGTATATT (SEQ ID NO: 780)	489
82	FGF1 (SEQ ID NO: 85)	AGTTGTGTTTAATTGGGAAGAG (SEQ ID NO: 782) CITATCCCATCCACTATACCAT (SEQ ID NO: 783)	420
83	GRIN2D (SEQ ID NO: 86)	ATAGTTTGTGGTTTGGATTTT (SEQ ID NO: 784) AAAACCTTTCCCTAACTTCAAT (SEQ ID NO: 785)	435
84	CTSB (SEQ ID NO: 87)	AAAATTCATCAAATAACCATAA (SEQ ID NO: 787) AAAAAGGAAGGTAGTAGGATTGT (SEQ ID NO: 786)	450
85	CTSD (SEQ ID NO: 88)	ATACAACCCTCCAACCTTCTAC (SEQ ID NO: 789) AAGGGGTTTTTAAGGAAATG (SEQ ID NO: 788)	498
86	PLAUR (SEQ ID NO: 89)	TGGTTAAAATGGAGGGTTTAAT (SEQ ID NO: 790) CCCCAAATTACCTAAATACAAA (SEQ ID NO: 791)	348
87	PSA (SEQ ID NO: 90)	TAAGAGAGAGGAGTTGAGGTTT (SEQ ID NO: 792) CCAAAATTAACCACCTACCTAA (SEQ ID NO: 793)	478

88	CGA (SEQ ID NO: 91)	TAGTGGTATAAGTTTGAAATGTT (SEQ ID NO: 794) TCCACCTACATCTAAACCCTAA (SEQ ID NO: 795)	364
89	CYP2D6 (SEQ ID NO: 92)	TAAGGGTTTGGAGTAGGAAGTA (SEQ ID NO: 796) CACATACAACAAAATTACCCAA (SEQ ID NO: 797)	403
90	CYP3A4 (SEQ ID NO: 93)	TATCACCACCTTCCCATATTA (SEQ ID NO: 799) GTTTGATGAATGGATTGTATGA (SEQ ID NO: 798)	484
91	TK1 (SEQ ID NO: 94)	ACCTCTACAAACATCTTATTCCA (SEQ ID NO: 801) TTGGGGGAGTTAGGTAGTATAG (SEQ ID NO: 800)	487
92	RENBP (SEQ ID NO: 95)	TTTGGTAGGGTTAAGGTTTTTA (SEQ ID NO: 802) CTTACTCATCCCTCCTACTCC (SEQ ID NO: 803)	350
93	F12 (SEQ ID NO: 96)	TAGGTTTAGGAGGGTAGTTTGA (SEQ ID NO: 804) CTCTCACAACCCAAAAATACA (SEQ ID NO: 805)	450
94	REN (SEQ ID NO: 97)	ACCTACTCCAAAAATCACAAAA (SEQ ID NO: 807) TATGTGGAAAAGTTAGGGTGIT (SEQ ID NO: 806)	489
95	EBAG9 (SEQ ID NO: 98)	CCAAAACATTAACCTCCCA (SEQ ID NO: 809) AATGTTTTAGAGGTTAGGGTTG (SEQ ID NO: 808)	463
96	MSMB (SEQ ID NO: 99)	GTTTGTAGGATGGTTTGATTT (SEQ ID NO: 810)	324

		TATATTACCTTATCCCCACCC (SEQ ID NO: 811)	
97	X15323 angiotensinogen gene 5' region and exon 1 (SEQ ID NO: 100)	AAACTCTCCCCTACCCTCTAC (SEQ ID NO: 813) GATGGAGTTGTTTTAGGTTGT (SEQ ID NO: 812)	374
98	ZNF147 (SEQ ID NO: 101)	TTTGTGTAAATAAGATGTGGGA (SEQ ID NO: 814) TAAACCCCTACAAAACCTACCAA (SEQ ID NO: 815)	484
99	EBBP (SEQ ID NO: 102)	GTATTTGTTTTTGGTGAGGGT (SEQ ID NO: 816) ATCATCTTCCTAAACATTCCAA (SEQ ID NO: 817)	482
100	CALR (SEQ ID NO: 103)	TAAATCACAACCATTAAACCAA (SEQ ID NO: 819) ATAAGAGGGGAGGAAGGTTTA (SEQ ID NO: 818)	490
101	BCAR1 (SEQ ID NO: 104)	AATTCTTCCTTCTATCTCCCTC (SEQ ID NO: 821) TTTATTTTGGGAAGGTTGTT (SEQ ID NO: 820)	499
102	COX7A2L (SEQ ID NO: 105)	AATCCTAAAAACCCTAACTTTTAAT (SEQ ID NO: 823) GGAGGTGTAAGGAGAATAGAGA (SEQ ID NO: 822)	398
103	AF174646 glandular kallikrein gene, promoter region and partial sequence (SEQ ID NO: 106)	CCAATTCATCATTCAACATCTA (SEQ ID NO: 825) ATTATTTGGGAGGATAGTGG (SEQ ID NO: 824)	325
104	KLK3 (SEQ ID	TTGGAGTGTAAGGATTAGGT (SEQ	387

	NO: 107)	ID NO: 826) AACCACATAATAACACAACCTCT (SEQ ID NO: 827)	
105	AKR1B1 (SEQ ID NO: 108)	CAACAAAAACATTCTTCTAAACTC (SEQ ID NO: 829) AGGTATTTAATTTTAGGATGGGT (SEQ ID NO: 828)	446
106	TGM4 (SEQ ID NO: 109)	AATCCTAACITTTAATCACCCA (SEQ ID NO: 831) GAGAGGGTAATGGTTTTAGGTA (SEQ ID NO: 830)	435
107	AR (SEQ ID NO: 110)	AATATAGGGAGGTTTAGGGTTT (SEQ ID NO: 832) TAACCATACATTCTCATCCAA (SEQ ID NO: 833)	424
108	HSPA1A (SEQ ID NO: 111)	AACCTTCAAATTCACAATCA (SEQ ID NO: 835) GGATTTATTGGAGGGGATAG (SEQ ID NO: 834)	495
109	FKBP4 (SEQ ID NO: 112)	TTTTTAAGTAGGGAAGGGTTT (SEQ ID NO: 836) TCCTTCTAACTACCTACCCCC (SEQ ID NO: 837)	308
110	ESR2 (SEQ ID NO: 113)	AAACCTTCCCAATAACCTCTTA (SEQ ID NO: 839) TAGAGGGGAGTAGTGTTTGAGT (SEQ ID NO: 838)	471
111	IGF1 (SEQ ID NO: 114)	TACCTTCTCCCAAATAATAA (SEQ ID NO: 841) GTATTAAAGGAATATGGGGGAT (SEQ ID NO: 840)	402
112	VTN (SEQ ID NO: 115)	GTTATTGGGTTAATGTAGGGA (SEQ ID NO: 842) TCTATCCCCTCAAACCTAAAAA (SEQ ID NO: 843)	492
113	CTSL (SEQ ID	CTACACCCACCCTTAAATAAAA (SEQ	328

	NO: 116)	ID NO: 845) T TAGTGGATT TGGAGGAAGTAG (SEQ ID NO: 844)	
114	TGFB3 (SEQ ID NO: 117)	CCTACTAAAAATCAAAACCCAA (SEQ ID NO: 847) AAGGTGGTGTAAAGTGGATAGAG (SEQ ID NO: 846)	369
115	MAPKAPK5 (SEQ ID NO: 118)	AAACCTACCTCCCCAACTAA (SEQ ID NO: 849) ATTTTGGTTTTAGGGTTGTAA (SEQ ID NO: 848)	495
116	PCAF (SEQ ID NO: 119)	GGATAAATGATTGAGAGGTTGT (SEQ ID NO: 850) CCTCCCTTAATTCTCCTACC (SEQ ID NO: 851)	369
117	NCOA3 (SEQ ID NO: 120)	AAGGGGGTGT TTTGTTAGATT (SEQ ID NO: 852) CCTAACCTACCCTTAATTTTT (SEQ ID NO: 853)	330
118	PRKCD (SEQ ID NO: 121)	CTTAACCCATCCCAATCA (SEQ ID NO: 855) GATAGAAGGATTTTAGTTTTATTGTT (SEQ ID NO: 854)	322

Table 2: Hybridisation oligonucleotides.

No:	Gene	Oligo:
1	ELK1 (SEQ ID NO: 10)	GTTTACGCGGAGTTTAGT (SEQ ID NO: 856)
2	ELK1 (SEQ ID NO: 10)	GTTTATGTGGAGTTTAGT (SEQ ID NO: 857)
3	ELK1 (SEQ ID NO: 10)	GTAGTATGGCGTGCGATA (SEQ ID NO: 858)
4	ELK1 (SEQ ID NO: 10)	GTAGTATGGTGTGTGATA (SEQ ID NO: 859)

5	ELK1 (SEQ ID NO: 10)	TTAATCGGCGTGGAGTAT (SEQ ID NO: 860)
6	ELK1 (SEQ ID NO: 10)	TTAATTGGTGTGGAGTAT (SEQ ID NO: 861)
7	GP1BB (SEQ ID NO: 7)	TTGAGAGCGGGTGGGAG (SEQ ID NO: 862)
8	GP1BB (SEQ ID NO: 7)	TTGAGAGTGGGTGGGAG (SEQ ID NO: 863)
9	GP1BB (SEQ ID NO: 7)	TTGGTTAGGTCGTAGTAT (SEQ ID NO: 864)
10	GP1BB (SEQ ID NO: 7)	TTGGTTAGGTTGTAGTAT (SEQ ID NO: 865)
11	GP1BB (SEQ ID NO: 7)	GTGGGAGCGGAAGTTGA (SEQ ID NO: 866)
12	GP1BB (SEQ ID NO: 7)	GTGGGAGTGGAAGTTGA (SEQ ID NO: 867)
13	GP1BB (SEQ ID NO: 7)	TGTTGGTGAACGTCGTAG (SEQ ID NO: 868)
14	GP1BB (SEQ ID NO: 7)	TGTTGGTGAATGTTGTAG (SEQ ID NO: 869)
15	GP1BB (SEQ ID NO: 7)	GGAGTTCGGTCGGGTTTT (SEQ ID NO: 870)
16	GP1BB (SEQ ID NO: 7)	GGAGTTTGTTGGGTTTT (SEQ ID NO: 871)
17	GP1BB (SEQ ID NO: 7)	TAGGTCGATTCGGTTGA (SEQ ID NO: 872)
18	GP1BB (SEQ ID NO: 7)	TAGGTTGATTGGGTTGA (SEQ ID NO: 873)
19	WT1 (SEQ ID NO: 8)	TAGTGAGACGAGGTTTT (SEQ ID NO: 874)
20	WT1 (SEQ ID NO: 8)	TAGTGAGATGAGGTTTT (SEQ ID NO: 875)
21	WT1 (SEQ ID NO: 8)	ATTGAGGGACGTTCTTT (SEQ ID NO: 876)

	NO: 8)	
22	WT1 (SEQ ID NO: 8)	ATTGAGGGATGTTTGT (SEQ ID NO: 877)
23	WT1 (SEQ ID NO: 8)	GTATTCGATTTTGTTCGGA (SEQ ID NO: 878)
24	WT1 (SEQ ID NO: 8)	GTATTGATTTTGTTCGGA (SEQ ID NO: 879)
25	WT1 (SEQ ID NO: 8)	GTAGGCGGTAATCGTTT (SEQ ID NO: 880)
26	WT1 (SEQ ID NO: 8)	GTAGGTGGTAATTGTTT (SEQ ID NO: 881)
27	APC (SEQ ID NO: 11)	GGGTTTCGTTTAATCGTAT (SEQ ID NO: 882)
28	APC (SEQ ID NO: 11)	GGGTTTGTTTAATTGTAT (SEQ ID NO: 883)
29	APC (SEQ ID NO: 11)	GGTTCGTATTTAGCGGATT (SEQ ID NO: 884)
30	APC (SEQ ID NO: 11)	GGTTGTATTTAGTGGATT (SEQ ID NO: 885)
31	APC (SEQ ID NO: 11)	TAGTTAATCGGCGGGTTT (SEQ ID NO: 886)
32	APC (SEQ ID NO: 11)	TAGTTAATTGGTGGGTTT (SEQ ID NO: 887)
33	APC (SEQ ID NO: 11)	TTTTCGAGTTCGGTAGTAT (SEQ ID NO: 888)
34	APC (SEQ ID NO: 11)	TTTTGAGTTTGGTAGTAT (SEQ ID NO: 889)
35	ARHI (SEQ ID NO: 12)	TTTTCGAGTAGCGTATTTG (SEQ ID NO: 890)
36	ARHI (SEQ ID NO: 12)	TTTTGAGTAGTGTATTTG (SEQ ID NO: 891)
37	ARHI (SEQ ID NO: 12)	ATAAGTGTGCGAGTTTAA (SEQ ID NO: 892)

38	ARHI (SEQ ID NO: 12)	ATAAGTGTGTGAGTTTAA (SEQ ID NO: 893)
39	ARHI (SEQ ID NO: 12)	TATAGTTGCGTAGGTAGT (SEQ ID NO: 894)
40	ARHI (SEQ ID NO: 12)	TATAGTTGTGTAGGTAGT (SEQ ID NO: 895)
41	BCL2 (SEQ ID NO: 13)	TGTTTCGCGTGATTGAAG (SEQ ID NO: 896)
42	BCL2 (SEQ ID NO: 13)	TGTTTTGTGTGATTGAAG (SEQ ID NO: 897)
43	BCL2 (SEQ ID NO: 13)	AGGGTACGATAATCGGGA (SEQ ID NO: 898)
44	BCL2 (SEQ ID NO: 13)	AGGGTATGATAATTGGGA (SEQ ID NO: 899)
45	BCL2 (SEQ ID NO: 13)	GGATTCGGTCGTTAGGAT (SEQ ID NO: 900)
46	BCL2 (SEQ ID NO: 13)	GGATTTGGTTGTTAGGAT (SEQ ID NO: 901)
47	BCL2 (SEQ ID NO: 13)	GATTTCGTCGAGATGTTA (SEQ ID NO: 902)
48	BCL2 (SEQ ID NO: 13)	GATTTTGTGAGATGTTA (SEQ ID NO: 903)
49	BRCA1 (SEQ ID NO: 14)	ATAAGCGCGTATAGGTTTT (SEQ ID NO: 904)
50	BRCA1 (SEQ ID NO: 14)	ATAAGTGTGTATAGGTTTT (SEQ ID NO: 905)
51	BRCA1 (SEQ ID NO: 14)	TTTCGTAACGTATGTTGGA (SEQ ID NO: 906)
52	BRCA1 (SEQ ID NO: 14)	TTTTGTAATGTATGTTGGA (SEQ ID NO: 907)
53	BRCA1 (SEQ ID NO: 14)	AATAAGTCGTAATTGGAAG (SEQ ID NO: 908)
54	BRCA1 (SEQ ID NO: 14)	AATAAGTTGTAATTGGAAG (SEQ ID NO: 909)

	NO: 14)	
55	BRCA1 (SEQ ID NO: 14)	TTTACGTTATTCGGGGGTA (SEQ ID NO: 910)
56	BRCA1 (SEQ ID NO: 14)	TTTATGTTATTTGGGGGTA (SEQ ID NO: 911)
57	CALCA (SEQ ID NO: 15)	TATAGCGGCGGGAATAAG (SEQ ID NO: 912)
58	CALCA (SEQ ID NO: 15)	TATAGTGGTGGGAATAAG (SEQ ID NO: 913)
59	CALCA (SEQ ID NO: 15)	TTGTTAGTTCGCGATTATA (SEQ ID NO: 914)
60	CALCA (SEQ ID NO: 15)	TTGTTAGTTGTGATTATA (SEQ ID NO: 915)
61	CALCA (SEQ ID NO: 15)	TTTAGGGATCGCGTATAGA (SEQ ID NO: 916)
62	CALCA (SEQ ID NO: 15)	TTTAGGGATTGTGTATAGA (SEQ ID NO: 917)
63	CALCA (SEQ ID NO: 15)	AAATTTTTCGTAGACGGTG (SEQ ID NO: 918)
64	CALCA (SEQ ID NO: 15)	AAATTTTGTAGATGGTG (SEQ ID NO: 919)
65	CCND2 (SEQ ID NO: 16)	GGATCGCGTTTGAAGTTG (SEQ ID NO: 920)
66	CCND2 (SEQ ID NO: 16)	GGATTGTGTTTGAAGTTG (SEQ ID NO: 921)
67	CCND2 (SEQ ID NO: 16)	TTTAATAACGAGAGGGG (SEQ ID NO: 922)
68	CCND2 (SEQ ID NO: 16)	TTTAATAATGAGAGGGG (SEQ ID NO: 923)
69	CCND2 (SEQ ID NO: 16)	TATCGTTTTAGAGCGGAGA (SEQ ID NO: 924)
70	CCND2 (SEQ ID NO: 16)	TATTGTTTTAGAGTGGAGA (SEQ ID NO: 925)

71	CDH1 (SEQ ID NO: 17)	TTGGGATTCTGAATTTAGT (SEQ ID NO: 926)
72	CDH1 (SEQ ID NO: 17)	TTGGGATTGAATTTAGT (SEQ ID NO: 927)
73	CDH1 (SEQ ID NO: 17)	GAGGGTTATCGCGTTTAT (SEQ ID NO: 928)
74	CDH1 (SEQ ID NO: 17)	GAGGGTTATTGTGTTTAT (SEQ ID NO: 929)
75	CDH1 (SEQ ID NO: 17)	TTAATTAGCGGTACGGGG (SEQ ID NO: 930)
76	CDH1 (SEQ ID NO: 17)	TTAATTAGTGGTATGGGG (SEQ ID NO: 931)
77	CDH1 (SEQ ID NO: 17)	TTTAGTGGCGTCGGAATT (SEQ ID NO: 932)
78	CDH1 (SEQ ID NO: 17)	TTTAGTGGTGTGGAATT (SEQ ID NO: 933)
79	CDKN1B (SEQ ID NO: 18)	GTTATAATTTCTGGGAAAGA (SEQ ID NO: 934)
80	CDKN1B (SEQ ID NO: 18)	GTTATAATTTTGGGAAAGA (SEQ ID NO: 935)
81	CDKN1B (SEQ ID NO: 18)	GGACGAGTTTTTATACGTAG (SEQ ID NO: 936)
82	CDKN1B (SEQ ID NO: 18)	GGATGAGTTTTTATATGTAG (SEQ ID NO: 937)
83	CDKN1B (SEQ ID NO: 18)	TTTGATTTCTGAGGGGAGT (SEQ ID NO: 938)
84	CDKN1B (SEQ ID NO: 18)	TTTGATTTGAGGGGAGT (SEQ ID NO: 939)
85	CDKN1B (SEQ ID NO: 18)	AAGAGAAACGTTGGAATA (SEQ ID NO: 940)
86	CDKN1B (SEQ ID NO: 18)	AAGAGAAATGTTGGAATA (SEQ ID NO: 941)
87	CDKN1B (SEQ ID NO: 18)	TAGTATCGGACGTTAGGAT (SEQ ID NO: 942)

	ID NO: 18)	
88	CDKN1B (SEQ ID NO: 18)	TAGTATTGGATGTTAGGAT (SEQ ID NO: 943)
89	CDKN2A (SEQ ID NO: 19)	TTTTTAGTCGTATAGGTGA (SEQ ID NO: 944)
90	CDKN2A (SEQ ID NO: 19)	TTTTTAGTTGTATAGGTGA (SEQ ID NO: 945)
91	CDKN2A (SEQ ID NO: 19)	GTTGTATCGCGGAGGAAG (SEQ ID NO: 946)
92	CDKN2A (SEQ ID NO: 19)	GTTGTATTGTGGAGGAAG (SEQ ID NO: 947)
93	CDKN2A (SEQ ID NO: 19)	ATTCGTTAAGTGTTCGGAG (SEQ ID NO: 948)
94	CDKN2A (SEQ ID NO: 19)	ATTTGTTAAGTGTTCGGAG (SEQ ID NO: 949)
95	CDKN2A (SEQ ID NO: 19)	GAAAGATATCGCGGTTTT (SEQ ID NO: 950)
96	CDKN2A (SEQ ID NO: 19)	GAAAGATATTGTGGTTTT (SEQ ID NO: 951)
97	CDKN2A (SEQ ID NO: 19)	TTTCGTTAGTATCGGAGG (SEQ ID NO: 952)
98	CDKN2A (SEQ ID NO: 19)	TTTGTTAGTATTGGAGG (SEQ ID NO: 953)
99	CDKN2A (SEQ ID NO: 19)	GGAGTTTTCGGTTGATTG (SEQ ID NO: 954)
100	CDKN2A (SEQ ID NO: 19)	GGAGTTTTTGGTTGATTG (SEQ ID NO: 955)
101	CDKN2A (SEQ ID NO: 19)	GGGCGTTGTTTAACGTAT (SEQ ID NO: 956)
102	CDKN2A (SEQ ID NO: 19)	GGGTGTTGTTTAATGTAT (SEQ ID NO: 957)
103	CDKN2A (SEQ ID NO: 19)	AATAGTTACGGTCGGAGG (SEQ ID NO: 958)

104	CDKN2A (SEQ ID NO: 19)	AATAGTTATGGTTGGAGG (SEQ ID NO: 959)
105	CDKN2A (SEQ ID NO: 19)	GGTCGGAGGTCGATTAG (SEQ ID NO: 960)
106	CDKN2A (SEQ ID NO: 19)	GGTTGGAGGTTGATTAG (SEQ ID NO: 961)
107	CDKN2B (SEQ ID NO: 20)	GGTTTTTCGGCGATTATAG (SEQ ID NO: 962)
108	CDKN2B (SEQ ID NO: 20)	GGTTTTTGGTGATTATAG (SEQ ID NO: 963)
109	CDKN2B (SEQ ID NO: 20)	AAAGTTCGGAGTTAACGAT (SEQ ID NO: 964)
110	CDKN2B (SEQ ID NO: 20)	AAAGTTTGGAGTTAATGAT (SEQ ID NO: 965)
111	CDKN2B (SEQ ID NO: 20)	AGTTTACGGTTAACGGTG (SEQ ID NO: 966)
112	CDKN2B (SEQ ID NO: 20)	AGTTTATGGTTAATGGTG (SEQ ID NO: 967)
113	CDKN2B (SEQ ID NO: 20)	AATGCGCGAGGAGAATAA (SEQ ID NO: 968)
114	CDKN2B (SEQ ID NO: 20)	AATGTGTGAGGAGAATAA (SEQ ID NO: 969)
115	CD44 (SEQ ID NO: 21)	AAGGTTTTACGGTTCGGT (SEQ ID NO: 970)
116	CD44 (SEQ ID NO: 21)	AAGGTTTATGTTTGGT (SEQ ID NO: 971)
117	CD44 (SEQ ID NO: 21)	GTGGGGTTCGGAGGTATA (SEQ ID NO: 972)
118	CD44 (SEQ ID NO: 21)	GTGGGGTTTGGAGGTATA (SEQ ID NO: 973)
119	CD44 (SEQ ID NO: 21)	GGTATTTTCGCGATATTTAG (SEQ ID NO: 974)
120	CD44 (SEQ ID	GGTATTTTGTGATATTTAG (SEQ ID NO: 975)

	NO: 21)	
121	CD44 (SEQ ID NO: 21)	GTTCTGTTTCGGATATTATGG (SEQ ID NO: 976)
122	CD44 (SEQ ID NO: 21)	GTTTGTTTTGGATATTATGG (SEQ ID NO: 977)
123	CD44 (SEQ ID NO: 21)	TTGGCGTAGATCGGTGA (SEQ ID NO: 978)
124	CD44 (SEQ ID NO: 21)	TTGGTG TAGATTGGTGA (SEQ ID NO: 979)
125	CSPG2 (SEQ ID NO: 22)	TTGGGTAACGTCGAATTT (SEQ ID NO: 980)
126	CSPG2 (SEQ ID NO: 22)	TTGGGTAATGTTGAATTT (SEQ ID NO: 981)
127	CSPG2 (SEQ ID NO: 22)	TAATAAGTCGTTTTTTAAGG (SEQ ID NO: 982)
128	CSPG2 (SEQ ID NO: 22)	TAATAAGTTGTTTTTTAAGG (SEQ ID NO: 983)
129	CSPG2 (SEQ ID NO: 22)	AAAATTCGCGAGTTTAGAAA (SEQ ID NO: 984)
130	CSPG2 (SEQ ID NO: 22)	AAAATTTGTGAGTTTAGAAA (SEQ ID NO: 985)
131	DAPK1 (SEQ ID NO: 23)	GAAGGGAGCGTATTTTAT (SEQ ID NO: 986)
132	DAPK1 (SEQ ID NO: 23)	GAAGGGAGTG TATTTTAT (SEQ ID NO: 987)
133	DAPK1 (SEQ ID NO: 23)	TGTTTTTCGGAAATTTGT (SEQ ID NO: 988)
134	DAPK1 (SEQ ID NO: 23)	TGTTTTTTGGAAATTTGT (SEQ ID NO: 989)
135	DAPK1 (SEQ ID NO: 23)	TTTCGTTTCGAGATGTGTA (SEQ ID NO: 990)
136	DAPK1 (SEQ ID NO: 23)	TTTGTTTTGAGATGTGTA (SEQ ID NO: 991)

137	DAPK1 (SEQ ID NO: 23)	GGAAATACGGTTTTTTCGTT (SEQ ID NO: 992)
138	DAPK1 (SEQ ID NO: 23)	GGAAATATGGTTTTTTTGTT (SEQ ID NO: 993)
139	GGT1 (SEQ ID NO: 24)	TATATTATCGGTTTATAGTT (SEQ ID NO: 994)
140	GGT1 (SEQ ID NO: 24)	TATATTATTGGTTTATAGTT (SEQ ID NO: 995)
141	GGT1 (SEQ ID NO: 24)	GGGATTTTATTCGTAGATTA (SEQ ID NO: 996)
142	GGT1 (SEQ ID NO: 24)	GGGATTTTATTGTAGATTA (SEQ ID NO: 997)
143	GGT1 (SEQ ID NO: 24)	GAGGTTAGACGTTTGTGA (SEQ ID NO: 998)
144	GGT1 (SEQ ID NO: 24)	GAGGTTAGATGTTTGTGA (SEQ ID NO: 999)
145	GGT1 (SEQ ID NO: 24)	TAGATATCGTTTTTGTGG (SEQ ID NO: 1000)
146	GGT1 (SEQ ID NO: 24)	TAGATATTGTTTTTGTGG (SEQ ID NO: 1001)
147	GSTP1 (SEQ ID NO: 25)	GGTTTTTTCGGTTAGTTG (SEQ ID NO: 1002)
148	GSTP1 (SEQ ID NO: 25)	GGTTTTTTTGGTTAGTTG (SEQ ID NO: 1003)
149	GSTP1 (SEQ ID NO: 25)	TTTAGGGCGTTTTTTG (SEQ ID NO: 1004)
150	GSTP1 (SEQ ID NO: 25)	TTTAGGGTGTTTTTTG (SEQ ID NO: 1005)
151	GSTP1 (SEQ ID NO: 25)	AGTTCGCGGGATTTTTTA (SEQ ID NO: 1006)
152	GSTP1 (SEQ ID NO: 25)	AGTTTGTGGGATTTTTTA (SEQ ID NO: 1007)
153	GSTP1 (SEQ ID NO: 25)	TAGTTTTCGTTATTAGTGAG (SEQ ID NO: 1008)

	NO: 25)	
154	GSTP1 (SEQ ID NO: 25)	TAGTTTTTGTTATTAGTGAG (SEQ ID NO: 1009)
155	HIC1 (SEQ ID NO: 26)	GAAGTTTACGCGGGATT (SEQ ID NO: 1010)
156	HIC1 (SEQ ID NO: 26)	GAAGTTTATGTGGGATT (SEQ ID NO: 1011)
157	HIC1 (SEQ ID NO: 26)	TAAAACGGCGTATAGGGG (SEQ ID NO: 1012)
158	HIC1 (SEQ ID NO: 26)	TAAAATGGTGTATAGGGG (SEQ ID NO: 1013)
159	HIC1 (SEQ ID NO: 26)	TTTATGTCGTTTGATGAT (SEQ ID NO: 1014)
160	HIC1 (SEQ ID NO: 26)	TTTATGTTGTTTGATGAT (SEQ ID NO: 1015)
161	HIC1 (SEQ ID NO: 26)	TAGGAGATTCGAAAGTTA (SEQ ID NO: 1016)
162	HIC1 (SEQ ID NO: 26)	TAGGAGATTGAAAGTTA (SEQ ID NO: 1017)
163	STMN1 (SEQ ID NO: 27)	GTTATCGGTTTCGGAATT (SEQ ID NO: 1816)
164	STMN1 (SEQ ID NO: 27)	GTTATTGGTTTGGGAATT (SEQ ID NO: 1817)
165	STMN1 (SEQ ID NO: 27)	GTAAGAACGTATATAGTGAG (SEQ ID NO: 1818)
166	STMN1 (SEQ ID NO: 27)	GTAAGAATGTATATAGTGAG (SEQ ID NO: 1819)
167	STMN1 (SEQ ID NO: 27)	AGAAATTACGATGATGTTAT (SEQ ID NO: 1820)
168	STMN1 (SEQ ID NO: 27)	AGAAATTATGATGATGTTAT (SEQ ID NO: 1821)
169	STMN1 (SEQ ID NO: 27)	ATGGGTGATACGTCGGTG (SEQ ID NO: 1822)

170	STMN1 (SEQ ID NO: 27)	ATGGGTGATATGTTGGTG (SEQ ID NO: 1823)
171	STK11 (SEQ ID NO: 28)	GGGTTAAGCGTCGATTAAT (SEQ ID NO: 1018)
172	STK11 (SEQ ID NO: 28)	GGGTTAAGTGTTGATTAAT (SEQ ID NO: 1019)
173	STK11 (SEQ ID NO: 28)	AGGGAGGTCGTTGGTATT (SEQ ID NO: 1020)
174	STK11 (SEQ ID NO: 28)	AGGGAGGTTGTTGGTATT (SEQ ID NO: 1021)
175	STK11 (SEQ ID NO: 28)	GGTATTCGTGATTACGATT (SEQ ID NO: 1022)
176	STK11 (SEQ ID NO: 28)	GGTATTTGTGATTATGATT (SEQ ID NO: 1023)
177	STK11 (SEQ ID NO: 28)	TTTCGAGTTTTATCGAGGT (SEQ ID NO: 1024)
178	STK11 (SEQ ID NO: 28)	TTTTGAGTTTTATTGAGGT (SEQ ID NO: 1025)
179	STK11 (SEQ ID NO: 28)	ATTAATGAGCGCGTTGTAT (SEQ ID NO: 1026)
180	STK11 (SEQ ID NO: 28)	ATTAATGAGTGTGTTGTAT (SEQ ID NO: 1027)
181	ING4 (SEQ ID NO: 29)	TAGTGACGAGAAGGTTAT (SEQ ID NO: 1028)
182	ING4 (SEQ ID NO: 29)	TAGTGATGAGAAGGTTAT (SEQ ID NO: 1029)
183	ING4 (SEQ ID NO: 29)	AATTATGAAGCGTTTTG (SEQ ID NO: 1030)
184	ING4 (SEQ ID NO: 29)	AATTATGAAGTGTTTTG (SEQ ID NO: 1031)
185	ING4 (SEQ ID NO: 29)	TTAGAGACGTGTTTGAA (SEQ ID NO: 1032)
186	ING4 (SEQ ID NO: 29)	TTAGAGATGTGTTTGAA (SEQ ID NO: 1033)

	NO: 29)	
187	MGMT (SEQ ID NO: 30)	TTAGGTTATCGGTGATTG (SEQ ID NO: 1034)
188	MGMT (SEQ ID NO: 30)	TTAGGTTATTGGTGATTG (SEQ ID NO: 1035)
189	MGMT (SEQ ID NO: 30)	TTGGACGGTATCGTTTAT (SEQ ID NO: 1036)
190	MGMT (SEQ ID NO: 30)	TTGGATGGTATTGTTTAT (SEQ ID NO: 1037)
191	MGMT (SEQ ID NO: 30)	TAGTCGTTTCGAGTAGGAT (SEQ ID NO: 1038)
192	MGMT (SEQ ID NO: 30)	TAGTTGTTTTGAGTAGGAT (SEQ ID NO: 1039)
193	MGMT (SEQ ID NO: 30)	AGTAGGATCGGGATTTTT (SEQ ID NO: 1040)
194	MGMT (SEQ ID NO: 30)	AGTAGGATTGGGATTTTT (SEQ ID NO: 1041)
195	MGMT (SEQ ID NO: 30)	TTATTCGGGTACGTGGTA (SEQ ID NO: 1042)
196	MGMT (SEQ ID NO: 30)	TTATTGGGTATGTGGTA (SEQ ID NO: 1043)
197	MLH1 (SEQ ID NO: 31)	ATAAGTTCGGTTTCGGTAT (SEQ ID NO: 1044)
198	MLH1 (SEQ ID NO: 31)	ATAAGTTGGTTTTGGTAT (SEQ ID NO: 1045)
199	MLH1 (SEQ ID NO: 31)	AAGAGCGGATAGCGATTT (SEQ ID NO: 1046)
200	MLH1 (SEQ ID NO: 31)	AAGAGTGGATAGTGATTT (SEQ ID NO: 1047)
201	MLH1 (SEQ ID NO: 31)	GAACGTGAGTACGAGGTA (SEQ ID NO: 1048)
202	MLH1 (SEQ ID NO: 31)	GAATGTGAGTATGAGGTA (SEQ ID NO: 1049)

203	MLH1 (SEQ ID NO: 31)	TAAAATGTCGTTCTGGT (SEQ ID NO: 1050)
204	MLH1 (SEQ ID NO: 31)	TAAAATGTTGTTGTGGT (SEQ ID NO: 1051)
205	CA9 (SEQ ID NO: 32)	TATGGTTTCGATAATTTTT (SEQ ID NO: 1052)
206	CA9 (SEQ ID NO: 32)	TATGGTTTGATAATTTTT (SEQ ID NO: 1053)
207	CA9 (SEQ ID NO: 32)	ATATATCGTGTGTGGGA (SEQ ID NO: 1054)
208	CA9 (SEQ ID NO: 32)	ATATATTGTGTGTGGGA (SEQ ID NO: 1055)
209	CA9 (SEQ ID NO: 32)	ATAGTTAGTCGTATGGTTT (SEQ ID NO: 1056)
210	CA9 (SEQ ID NO: 32)	ATAGTTAGTTGTATGGTTT (SEQ ID NO: 1057)
211	MYC (SEQ ID NO: 33)	GGGATCGCGTTGAGTATA (SEQ ID NO: 1058)
212	MYC (SEQ ID NO: 33)	GGGATTGTGTGAGTATA (SEQ ID NO: 1059)
213	MYC (SEQ ID NO: 33)	GAGATTCGGAGCGAATAG (SEQ ID NO: 1060)
214	MYC (SEQ ID NO: 33)	GAGATTGGAGTGAATAG (SEQ ID NO: 1061)
215	MYC (SEQ ID NO: 33)	AGTTAGCGGTTCTAATTT (SEQ ID NO: 1062)
216	MYC (SEQ ID NO: 33)	AGTTAGTGTTTGAATTT (SEQ ID NO: 1063)
217	MYC (SEQ ID NO: 33)	GAGTAAGGACGCGATTTT (SEQ ID NO: 1064)
218	MYC (SEQ ID NO: 33)	GAGTAAGGATGTGATTTT (SEQ ID NO: 1065)
219	N33 (SEQ ID NO: 33)	TTGGTTCGGGAAAGGTAA (SEQ ID NO: 1066)

	35)	
220	N33 (SEQ ID NO: 35)	TTGGTTTGGGAAAGGTAA (SEQ ID NO: 1067)
221	N33 (SEQ ID NO: 35)	TTTTCGGTGAATCGGATG (SEQ ID NO: 1068)
222	N33 (SEQ ID NO: 35)	TTTTGGTGAATTGGATG (SEQ ID NO: 1069)
223	N33 (SEQ ID NO: 35)	TGTTATTTTCGGAGGGTTT (SEQ ID NO: 1070)
224	N33 (SEQ ID NO: 35)	TGTTATTTTGGAGGGTTT (SEQ ID NO: 1071)
225	N33 (SEQ ID NO: 35)	GTTTAGTTAGCGGGTTTT (SEQ ID NO: 1072)
226	N33 (SEQ ID NO: 35)	GTTTAGTTAGTGGGTTTT (SEQ ID NO: 1073)
227	N33 (SEQ ID NO: 35)	TTTTTTACGTCGTAGGTAAG (SEQ ID NO: 1074)
228	N33 (SEQ ID NO: 35)	TTTTTTATGTTGTAGGTAAG (SEQ ID NO: 1075)
229	N33 (SEQ ID NO: 35)	ATTTAGTTCGGGGGAGGA (SEQ ID NO: 1076)
230	N33 (SEQ ID NO: 35)	ATTTAGTTTGGGGGAGGA (SEQ ID NO: 1077)
231	PAX6 (SEQ ID NO: 36)	GAGGGTTATGCGATTTA (SEQ ID NO: 1078)
232	PAX6 (SEQ ID NO: 36)	GAGGGTTATGTGATTTA (SEQ ID NO: 1079)
233	PAX6 (SEQ ID NO: 36)	TATTGTTTCGGTTGTTAG (SEQ ID NO: 1080)
234	PAX6 (SEQ ID NO: 36)	TATTGTTTTGGTTGTTAG (SEQ ID NO: 1081)
235	PAX6 (SEQ ID NO: 36)	TTAGTAGCGAGTTTAGGT (SEQ ID NO: 1082)

236	PAX6 (SEQ ID NO: 36)	TTAGTAGTGAGTTTAGGT (SEQ ID NO: 1083)
237	PAX6 (SEQ ID NO: 36)	GTTTAGGTCGCGTAGATTT (SEQ ID NO: 1084)
238	PAX6 (SEQ ID NO: 36)	GTTTAGGTTGTGTAGATTT (SEQ ID NO: 1085)
239	PAX6 (SEQ ID NO: 36)	AGTTTAGCGTATTTTCGGT (SEQ ID NO: 1086)
240	PAX6 (SEQ ID NO: 36)	AGTTTAGTGTATTTTGGT (SEQ ID NO: 1087)
241	X51730 PGR (SEQ ID NO: 67)	TGTATCGAGAGGTTTCGATT (SEQ ID NO: 1088)
242	X51730 PGR (SEQ ID NO: 67)	TGTATTGAGAGGTTTGATT (SEQ ID NO: 1089)
243	X51730 PGR (SEQ ID NO: 67)	AGGAGTCGCGTGTTATTA (SEQ ID NO: 1090)
244	X51730 PGR (SEQ ID NO: 67)	AGGAGTTGTGTGTTATTA (SEQ ID NO: 1091)
245	X51730 PGR (SEQ ID NO: 67)	GTTAGGAGACGAGATTTT (SEQ ID NO: 1092)
246	X51730 PGR (SEQ ID NO: 67)	GTTAGGAGATGAGATTTT (SEQ ID NO: 1093)
247	X51730 PGR (SEQ ID NO: 67)	TGTCGTTTCGTTGGGATAA (SEQ ID NO: 1094)
248	X51730 PGR (SEQ ID NO: 67)	TGTTGTTTGTGTTGGGATAA (SEQ ID NO: 1095)
249	PTEN (SEQ ID NO: 38)	TTGCGTTTCGTATTTAGAG (SEQ ID NO: 1096)
250	PTEN (SEQ ID NO: 38)	TTTGTTTGTATTTAGAG (SEQ ID NO: 1097)
251	PTEN (SEQ ID NO: 38)	TTAGAGTTATCGTTTTGTT (SEQ ID NO: 1098)
252	PTEN (SEQ ID NO: 38)	TTAGAGTTATTGTTTTGTT (SEQ ID NO: 1099)

	NO: 38)	
253	PTEN (SEQ ID NO: 38)	TGATGTGGCGGGATTTTT (SEQ ID NO: 1100)
254	PTEN (SEQ ID NO: 38)	TGATGTGGTGGGATTTTT (SEQ ID NO: 1101)
255	PTEN (SEQ ID NO: 38)	TTTTTCGGAAGTTGTAG (SEQ ID NO: 1102)
256	PTEN (SEQ ID NO: 38)	TTTTTTGGAAGTTGTAG (SEQ ID NO: 1103)
257	RARB (SEQ ID NO: 39)	TAGTAGTTCGGGTAGGGT (SEQ ID NO: 1104)
258	RARB (SEQ ID NO: 39)	TAGTAGTTTGGGTAGGGT (SEQ ID NO: 1105)
259	RARB (SEQ ID NO: 39)	AGGGTTTATCGAAAGTTT (SEQ ID NO: 1106)
260	RARB (SEQ ID NO: 39)	AGGGTTTATTGAAAGTTT (SEQ ID NO: 1107)
261	RARB (SEQ ID NO: 39)	GAGCGATTTCGAGTAGGGT (SEQ ID NO: 1108)
262	RARB (SEQ ID NO: 39)	GAGTGATTTGAGTAGGGT (SEQ ID NO: 1109)
263	RARB (SEQ ID NO: 39)	GTATCGTCGGGTAGGAT (SEQ ID NO: 1110)
264	RARB (SEQ ID NO: 39)	GTATTGTTGGGTAGGAT (SEQ ID NO: 1111)
265	RARB (SEQ ID NO: 39)	GAACGTATTCGGAAGGTT (SEQ ID NO: 1112)
266	RARB (SEQ ID NO: 39)	GAATGTATTTGGAAGGTT (SEQ ID NO: 1113)
267	SFN (SEQ ID NO: 40)	GAGTAGGTCGAACGTTAT (SEQ ID NO: 1114)
268	SFN (SEQ ID NO: 40)	GAGTAGGTTGAATGTTAT (SEQ ID NO: 1115)

269	SFN (SEQ ID NO: 40)	TTTGCGAAGAGCGAAATT (SEQ ID NO: 1116)
270	SFN (SEQ ID NO: 40)	TTTGTGAAGAGTGAAATT (SEQ ID NO: 1117)
271	SFN (SEQ ID NO: 40)	TAACGAGGAGGGTTCGGA (SEQ ID NO: 1118)
272	SFN (SEQ ID NO: 40)	TAATGAGGAGGGTTTGA (SEQ ID NO: 1119)
273	SFN (SEQ ID NO: 40)	GTTTCGAGGTGCGTGAGTA (SEQ ID NO: 1120)
274	SFN (SEQ ID NO: 40)	GTTTGAGGTGTGTGAGTA (SEQ ID NO: 1121)
275	S100A2 (SEQ ID NO: 41)	TTTAATTGCGTTGTGTG (SEQ ID NO: 1122)
276	S100A2 (SEQ ID NO: 41)	TTTAATTGTGTTGTGTG (SEQ ID NO: 1123)
277	S100A2 (SEQ ID NO: 41)	TATATAGGCGTATGTATG (SEQ ID NO: 1124)
278	S100A2 (SEQ ID NO: 41)	TATATAGGTGTATGTATG (SEQ ID NO: 1125)
279	S100A2 (SEQ ID NO: 41)	TATGTATACGAGTATTGGAT (SEQ ID NO: 1126)
280	S100A2 (SEQ ID NO: 41)	TATGTATATGAGTATTGGAT (SEQ ID NO: 1127)
281	S100A2 (SEQ ID NO: 41)	AGTTTACGCGTGTGTTA (SEQ ID NO: 1128)
282	S100A2 (SEQ ID NO: 41)	AGTTTAGTGTGTGTTA (SEQ ID NO: 1129)
283	TFF1 (SEQ ID NO: 42)	TATTTGGTCGAGGTTTA (SEQ ID NO: 1130)
284	TFF1 (SEQ ID NO: 42)	TATTTGGTTGAGGTTTA (SEQ ID NO: 1131)
285	TFF1 (SEQ ID NO: 42)	AGATAGAGACGTGTATAGT (SEQ ID NO: 1132)

	NO: 42)	
286	TFF1 (SEQ ID NO: 42)	AGATAGAGATGTGTATAGT (SEQ ID NO: 1133)
287	TFF1 (SEQ ID NO: 42)	TGGTTTTTCGTGAAAGAT (SEQ ID NO: 1134)
288	TFF1 (SEQ ID NO: 42)	TGGTTTTTGTGAAAGAT (SEQ ID NO: 1135)
289	TFF1 (SEQ ID NO: 42)	AATATTATCGACGTTTTT (SEQ ID NO: 1136)
290	TFF1 (SEQ ID NO: 42)	ATTATGATGTTTTTTTAGAA (SEQ ID NO: 1137)
291	TGFBR2 (SEQ ID NO: 43)	GAAAACGTGGACGTTTTT (SEQ ID NO: 1138)
292	TGFBR2 (SEQ ID NO: 43)	GAAAATGTGGATGTTTTT (SEQ ID NO: 1139)
293	TGFBR2 (SEQ ID NO: 43)	ATTTGGAGCGAGGAATTT (SEQ ID NO: 1140)
294	TGFBR2 (SEQ ID NO: 43)	ATTTGGAGTGAGGAATTT (SEQ ID NO: 1141)
295	TGFBR2 (SEQ ID NO: 43)	AGTTGAAAGTCGGTAAA (SEQ ID NO: 1142)
296	TGFBR2 (SEQ ID NO: 43)	AGTTGAAAGTTGGTAAA (SEQ ID NO: 1143)
297	TGFBR2 (SEQ ID NO: 43)	AAAGTTTTTCGGAGGGGTT (SEQ ID NO: 1144)
298	TGFBR2 (SEQ ID NO: 43)	AAAGTTTTTGGAGGGGTT (SEQ ID NO: 1145)
299	TGFBR2 (SEQ ID NO: 43)	GGTAGTTACGAGAGAGTT (SEQ ID NO: 1146)
300	TGFBR2 (SEQ ID NO: 43)	GGTAGTTATGAGAGAGTT (SEQ ID NO: 1147)
301	TIMP3 (SEQ ID NO: 44)	GTTTTTCGTTGGAGAAAA (SEQ ID NO: 1148)

302	TIMP3 (SEQ ID NO: 44)	GTTTTTTGTGGAGAAAA (SEQ ID NO: 1149)
303	TIMP3 (SEQ ID NO: 44)	GAAAAATATCGGTATTTTGG (SEQ ID NO: 1150)
304	TIMP3 (SEQ ID NO: 44)	GAAAAATATTGGTATTTTGG (SEQ ID NO: 1151)
305	TIMP3 (SEQ ID NO: 44)	ATGTGGGGCGCGGGGATA (SEQ ID NO: 1152)
306	TIMP3 (SEQ ID NO: 44)	ATGTGGGGTGTGGGGATA (SEQ ID NO: 1153)
307	TIMP3 (SEQ ID NO: 44)	GGGATAAGCGAATTTTTTA (SEQ ID NO: 1154)
308	TIMP3 (SEQ ID NO: 44)	GGGATAAGTGAATTTTTTA (SEQ ID NO: 1155)
309	VHL (SEQ ID NO: 45)	TATAAGCGTGATGATTGG (SEQ ID NO: 1156)
310	VHL (SEQ ID NO: 45)	TATAAGTGTGATGATTGG (SEQ ID NO: 1157)
311	VHL (SEQ ID NO: 45)	TTTCGTGTGAGATGCGTTA (SEQ ID NO: 1158)
312	VHL (SEQ ID NO: 45)	TTTTGTGTGAGATGTGTTA (SEQ ID NO: 1159)
313	VHL (SEQ ID NO: 45)	GAGATGCGTTATTTTCGAA (SEQ ID NO: 1160)
314	VHL (SEQ ID NO: 45)	GAGATGTGTTATTTTGA (SEQ ID NO: 1161)
315	VHL (SEQ ID NO: 45)	TATTGCGCGTTTGATATGA (SEQ ID NO: 1162)
316	VHL (SEQ ID NO: 45)	TATTGTGTGTTTGATATGA (SEQ ID NO: 1163)
317	CDKN1C (SEQ ID NO: 46)	ATGAAGAACGGTTAAGGG (SEQ ID NO: 1164)
318	CDKN1C (SEQ ID NO: 46)	ATGAAGAATGGTTAAGGG (SEQ ID NO: 1165)

	ID NO: 46)	
319	CDKN1C (SEQ ID NO: 46)	TATTTTCGAGTTAGGTCGAA (SEQ ID NO: 1166)
320	CDKN1C (SEQ ID NO: 46)	TATTTTGAGTTAGGTTGAA (SEQ ID NO: 1167)
321	CDKN1C (SEQ ID NO: 46)	AATTAGTCGGGGTCGTGA (SEQ ID NO: 1168)
322	CDKN1C (SEQ ID NO: 46)	AATTAGTTGGGGTTGTGA (SEQ ID NO: 1169)
323	CDKN1C (SEQ ID NO: 46)	TTAGTGTTCTGTTTGAAT (SEQ ID NO: 1170)
324	CDKN1C (SEQ ID NO: 46)	TTAGTGTTTGTGTTGAAT (SEQ ID NO: 1171)
325	CAV1 (SEQ ID NO: 47)	TAAATATTTTCGATTGTTGAT (SEQ ID NO: 1172)
326	CAV1 (SEQ ID NO: 47)	TTTAAATATTTTGATTGTTG (SEQ ID NO: 1173)
327	CAV1 (SEQ ID NO: 47)	TTGGTATCGTTGAAGAAT (SEQ ID NO: 1174)
328	CAV1 (SEQ ID NO: 47)	TTGGTATTGTTGAAGAAT (SEQ ID NO: 1175)
329	CAV1 (SEQ ID NO: 47)	TAAGACGCGTTTTTTTGA (SEQ ID NO: 1176)
330	CAV1 (SEQ ID NO: 47)	TAAGATGTGTTTTTTTGA (SEQ ID NO: 1177)
331	CAV1 (SEQ ID NO: 47)	AATACGTAGATTCGGAGGT (SEQ ID NO: 1178)
332	CAV1 (SEQ ID NO: 47)	AATATGTAGATTGGAGGT (SEQ ID NO: 1179)
333	CAV1 (SEQ ID NO: 47)	TAGATTCGGAGGTAGGTA (SEQ ID NO: 1180)
334	CAV1 (SEQ ID NO: 47)	TAGATTTGGAGGTAGGTA (SEQ ID NO: 1181)

335	CDH13 (SEQ ID NO: 48)	TAAACGAGGGAGCGTTA (SEQ ID NO: 1182)
336	CDH13 (SEQ ID NO: 48)	TAAAATGAGGGAGTGTTA (SEQ ID NO: 1183)
337	CDH13 (SEQ ID NO: 48)	AAGGAATTCGTTTGTAAA (SEQ ID NO: 1184)
338	CDH13 (SEQ ID NO: 48)	AAGGAATTGTTTGTAAA (SEQ ID NO: 1185)
339	CDH13 (SEQ ID NO: 48)	AAGTGGTCGTTAGTTTT (SEQ ID NO: 1186)
340	CDH13 (SEQ ID NO: 48)	AAGTGGTTGTTAGTTTT (SEQ ID NO: 1187)
341	NDRG1 (SEQ ID NO: 49)	GAGTAGGACGGTGTTAAG (SEQ ID NO: 1188)
342	NDRG1 (SEQ ID NO: 49)	GAGTAGGATGGTGTTAAG (SEQ ID NO: 1189)
343	NDRG1 (SEQ ID NO: 49)	TAAATTTAACGTTGGGTAG (SEQ ID NO: 1190)
344	NDRG1 (SEQ ID NO: 49)	TAAATTTAATGTTGGGTAG (SEQ ID NO: 1191)
345	NDRG1 (SEQ ID NO: 49)	GATAATGACGGTGTTAGT (SEQ ID NO: 1192)
346	NDRG1 (SEQ ID NO: 49)	GATAATGATGGTGTTAGT (SEQ ID NO: 1193)
347	NDRG1 (SEQ ID NO: 49)	GTTGTACGTTAGGAGTTA (SEQ ID NO: 1194)
348	NDRG1 (SEQ ID NO: 49)	GTTGTATGTTAGGAGTTA (SEQ ID NO: 1195)
349	PTGS2 (SEQ ID NO: 50)	TTATCGGGTTACGTAATT (SEQ ID NO: 1196)
350	PTGS2 (SEQ ID NO: 50)	TTATTGGGTTATGTAATT (SEQ ID NO: 1197)
351	PTGS2 (SEQ ID NO: 50)	GTACGAAAAGCGGAAAG (SEQ ID NO: 1198)

	NO: 50)	
352	PTGS2 (SEQ ID NO: 50)	GTATGAAAAGGTGGAAAG (SEQ ID NO: 1199)
353	PTGS2 (SEQ ID NO: 50)	ATTGGTTTTCGGAAGCGTT (SEQ ID NO: 1200)
354	PTGS2 (SEQ ID NO: 50)	ATTGGTTTTGGAAGTGTT (SEQ ID NO: 1201)
355	PTGS2 (SEQ ID NO: 50)	AAGCGTTCGGGTAAAGAT (SEQ ID NO: 1202)
356	PTGS2 (SEQ ID NO: 50)	AAGTGTTTGGGTAAAGAT (SEQ ID NO: 1203)
357	THBS1 (SEQ ID NO: 51)	TATTTTACGGGGACGGTG (SEQ ID NO: 1204)
358	THBS1 (SEQ ID NO: 51)	TATTTTATGGGGATGGTG (SEQ ID NO: 1205)
359	THBS1 (SEQ ID NO: 51)	GATTAGTTCGTTGAAAGT (SEQ ID NO: 1206)
360	THBS1 (SEQ ID NO: 51)	GATTAGTTTGTGAAAGT (SEQ ID NO: 1207)
361	THBS1 (SEQ ID NO: 51)	GTGGCGTAAGAGTACGAG (SEQ ID NO: 1208)
362	THBS1 (SEQ ID NO: 51)	GTGGTGTAAGAGTATGAG (SEQ ID NO: 1209)
363	TMEFF2 (SEQ ID NO: 52)	ATAGGTTACGGGTTGGAG (SEQ ID NO: 1210)
364	TMEFF2 (SEQ ID NO: 52)	ATAGGTTATGGGTTGGAG (SEQ ID NO: 1211)
365	TMEFF2 (SEQ ID NO: 52)	AAATTGCGAACGTTTGG (SEQ ID NO: 1212)
366	TMEFF2 (SEQ ID NO: 52)	AAATTGTGAATGTTTGG (SEQ ID NO: 1213)
367	TMEFF2 (SEQ ID NO: 52)	AAATGGAGTTCGTTTTT (SEQ ID NO: 1214)

368	TMEFF2 (SEQ ID NO: 52)	AAATGGAGTTTGTTTTTT (SEQ ID NO: 1215)
369	TMEFF2 (SEQ ID NO: 52)	GGTCGATGTTTCGGTAA (SEQ ID NO: 1216)
370	TMEFF2 (SEQ ID NO: 52)	GGTTGATGTTTTGGTAA (SEQ ID NO: 1217)
371	PLAU (SEQ ID NO: 53)	TGAGGTTTCGTTTAAAGA (SEQ ID NO: 1218)
372	PLAU (SEQ ID NO: 53)	TGAGGTTTTGTTTAAAGA (SEQ ID NO: 1219)
373	PLAU (SEQ ID NO: 53)	TTATTTACGTGTGTGGAG (SEQ ID NO: 1220)
374	PLAU (SEQ ID NO: 53)	TTATTTATGTGTGTGGAG (SEQ ID NO: 1221)
375	PLAU (SEQ ID NO: 53)	GGTGATTAGCGTTATATATT (SEQ ID NO: 1222)
376	PLAU (SEQ ID NO: 53)	GGTGATTAGTGTATATATT (SEQ ID NO: 1223)
377	PLAU (SEQ ID NO: 53)	GATAAGTCGTGTTTGAG (SEQ ID NO: 1224)
378	PLAU (SEQ ID NO: 53)	GATAAGTTGTGTTTGAG (SEQ ID NO: 1225)
379	TMEFF2 (SEQ ID NO: 54)	TAGTTCGTTCCGGTGAAGT (SEQ ID NO: 1226)
380	TMEFF2 (SEQ ID NO: 54)	TAGTTTGTTTGGTGAAGT (SEQ ID NO: 1227)
381	TMEFF2 (SEQ ID NO: 54)	GTGAAGTTCGTTGTTTT (SEQ ID NO: 1228)
382	TMEFF2 (SEQ ID NO: 54)	GTGAAGTTTGTTGTTTT (SEQ ID NO: 1229)
383	TMEFF2 (SEQ ID NO: 54)	TTAAACGTTTATCGGTTGG (SEQ ID NO: 1230)
384	TMEFF2 (SEQ ID NO: 54)	TTAAATGTTTATTGGTTGG (SEQ ID NO: 1231)

	NO: 54)	
385	TMEFF2 (SEQ ID NO: 54)	TTTAATTTCTAGAGAATA (SEQ ID NO: 1232)
386	TMEFF2 (SEQ ID NO: 54)	TTTAATTTGTAGAGAATA (SEQ ID NO: 1233)
387	TMEFF2 (SEQ ID NO: 54)	GAAGAATACGCGTATTTAGT (SEQ ID NO: 1234)
388	TMEFF2 (SEQ ID NO: 54)	GAAGAATATGTGTATTTAGT (SEQ ID NO: 1235)
389	DNMT1 (SEQ ID NO: 55)	GTACGGTGTTGAGGTAT (SEQ ID NO: 1236)
390	DNMT1 (SEQ ID NO: 55)	GTATGGTGTTGAGGTAT (SEQ ID NO: 1237)
391	DNMT1 (SEQ ID NO: 55)	TTTTACGCGGAGTAGTG (SEQ ID NO: 1238)
392	DNMT1 (SEQ ID NO: 55)	TTTTATGTGGAGTAGTG (SEQ ID NO: 1239)
393	DNMT1 (SEQ ID NO: 55)	GGGAATACGTATGCGTAAG (SEQ ID NO: 1240)
394	DNMT1 (SEQ ID NO: 55)	GGGAATATGTATGTGTAAG (SEQ ID NO: 1241)
395	DNMT1 (SEQ ID NO: 55)	GAACGGAGTCGGTTATGT (SEQ ID NO: 1242)
396	DNMT1 (SEQ ID NO: 55)	GAATGGAGTTGGTTATGT (SEQ ID NO: 1243)
397	DNMT1 (SEQ ID NO: 55)	AAACGGAGAGAGGCGATA (SEQ ID NO: 1244)
398	DNMT1 (SEQ ID NO: 55)	AAATGGAGAGAGGTGATA (SEQ ID NO: 1245)
399	ESR1 (SEQ ID NO: 70)	TTTTTTGGTCGTGAAATT (SEQ ID NO: 1246)
400	ESR1 (SEQ ID NO: 70)	TTTTTTGGTTGTGAAATT (SEQ ID NO: 1247)

401	ESR1 (SEQ ID NO: 70)	TTTAGTAGCGACGATAAGTA (SEQ ID NO: 1248)
402	ESR1 (SEQ ID NO: 70)	TTTAGTAGTGATGATAAGTA (SEQ ID NO: 1249)
403	ESR1 (SEQ ID NO: 70)	GGATCGTTTAAATCGAGT (SEQ ID NO: 1250)
404	ESR1 (SEQ ID NO: 70)	GGATTGTTTAAATTGAGT (SEQ ID NO: 1251)
405	ESR1 (SEQ ID NO: 70)	TGGAGGTTCTGGGAGTTTA (SEQ ID NO: 1252)
406	ESR1 (SEQ ID NO: 70)	TGGAGGTTTGGGAGTTTA (SEQ ID NO: 1253)
407	ESR1 (SEQ ID NO: 70)	TTTTATCGGATTCGTAGGT (SEQ ID NO: 1254)
408	ESR1 (SEQ ID NO: 70)	TTTTATTGGATTGTAGGT (SEQ ID NO: 1255)
409	APAF1 (SEQ ID NO: 57)	AGTAGGACGTGGTCGTTT (SEQ ID NO: 1256)
410	APAF1 (SEQ ID NO: 57)	AGTAGGATGTGGTTGTTT (SEQ ID NO: 1257)
411	APAF1 (SEQ ID NO: 57)	ATTCGGCGGGATTGATT (SEQ ID NO: 1258)
412	APAF1 (SEQ ID NO: 57)	ATTTGGTGGGATTGATT (SEQ ID NO: 1259)
413	APAF1 (SEQ ID NO: 57)	TAGCGAGTGGACGTGATT (SEQ ID NO: 1260)
414	APAF1 (SEQ ID NO: 57)	TAGTGAGTGGATGTGATT (SEQ ID NO: 1261)
415	HOXA5 (SEQ ID NO: 58)	AGTTAGTCGGGTTTAAAG (SEQ ID NO: 1262)
416	HOXA5 (SEQ ID NO: 58)	AGTTAGTTGGGTTTAAAG (SEQ ID NO: 1263)
417	HOXA5 (SEQ ID NO: 58)	ATATGGTTTTCGTGTATT (SEQ ID NO: 1264)

	NO: 58)	
418	HOXA5 (SEQ ID NO: 58)	ATATGGTTTTGTGTATT (SEQ ID NO: 1265)
419	HOXA5 (SEQ ID NO: 58)	TTTTGCGAGCGTATGAG (SEQ ID NO: 1266)
420	HOXA5 (SEQ ID NO: 58)	TTTTGTGAGTGTATGAG (SEQ ID NO: 1267)
421	RASSF1 (SEQ ID NO: 59)	GTTTCGGGGTTCGTAATA (SEQ ID NO: 1268)
422	RASSF1 (SEQ ID NO: 59)	GTTTTGGGGTTTGTAAATA (SEQ ID NO: 1269)
423	RASSF1 (SEQ ID NO: 59)	AGGTAGTTTTTCGAGAATG (SEQ ID NO: 1270)
424	RASSF1 (SEQ ID NO: 59)	AGGTAGTTTTTGAGAATG (SEQ ID NO: 1271)
425	RASSF1 (SEQ ID NO: 59)	TTTGTGTCGTCGGGAAAT (SEQ ID NO: 1272)
426	RASSF1 (SEQ ID NO: 59)	TTTGTGTTGTTGGGAAAT (SEQ ID NO: 1273)
427	RASSF1 (SEQ ID NO: 59)	TTAGTTTTTCGCGTAGAATTA (SEQ ID NO: 1274)
428	RASSF1 (SEQ ID NO: 59)	TTAGTTTTTGTGTAGAATTA (SEQ ID NO: 1275)
429	RASSF1 (SEQ ID NO: 59)	TATTTGCGGAGTCGGTAA (SEQ ID NO: 1276)
430	RASSF1 (SEQ ID NO: 59)	TATTTGTGGAGTTGGTAA (SEQ ID NO: 1277)
431	RASSF1 (SEQ ID NO: 59)	TTGTAGCGGGTGGAGTA (SEQ ID NO: 1278)
432	RASSF1 (SEQ ID NO: 59)	TTGTAGTGGGTGGAGTA (SEQ ID NO: 1279)
433	ABCB1 (SEQ ID NO: 1)	AAATGCGAATTCGAGAAA (SEQ ID NO: 1280)

434	ABCB1 (SEQ ID NO: 1)	AAATGTGAATTTTGAGAAA (SEQ ID NO: 1281)
435	ABCB1 (SEQ ID NO: 1)	TTCGTAGTTTTTCGAGGAA (SEQ ID NO: 1282)
436	ABCB1 (SEQ ID NO: 1)	TTTGTAGTTTTTGAGGAA (SEQ ID NO: 1283)
437	ABCB1 (SEQ ID NO: 1)	TAGTTAATTCGGGTCGGG (SEQ ID NO: 1284)
438	ABCB1 (SEQ ID NO: 1)	TAGTTAATTTGGGTTGGG (SEQ ID NO: 1285)
439	ABCB1 (SEQ ID NO: 1)	TGAGTATAGTCGTTTCGTT (SEQ ID NO: 1286)
440	ABCB1 (SEQ ID NO: 1)	TGAGTATAGTTGTTTTGTT (SEQ ID NO: 1287)
441	ABCB1 (SEQ ID NO: 1)	GTTTATTCGAGTAGCGGTT (SEQ ID NO: 1288)
442	ABCB1 (SEQ ID NO: 1)	GTTTATTTGAGTAGTGGTT (SEQ ID NO: 1289)
443	HLA-F (SEQ ID NO: 9)	AATTTTTGCGGTTTCGATAG (SEQ ID NO: 1290)
444	HLA-F (SEQ ID NO: 9)	AATTTTTGTGGTTTGATAG (SEQ ID NO: 1291)
445	HLA-F (SEQ ID NO: 9)	GGGCGTAGGTTACGATTA (SEQ ID NO: 1292)
446	HLA-F (SEQ ID NO: 9)	GGGTGTAGGTTATGATTA (SEQ ID NO: 1293)
447	HLA-F (SEQ ID NO: 9)	GAGTTTTCGGATTCGAAAT (SEQ ID NO: 1294)
448	HLA-F (SEQ ID NO: 9)	GAGTTTTGGATTTGAAAT (SEQ ID NO: 1295)
449	HLA-F (SEQ ID NO: 9)	GAACGAGGATTTGCGTTT (SEQ ID NO: 1296)
450	HLA-F (SEQ ID NO: 9)	GAATGAGGATTTGTGTTT (SEQ ID NO: 1297)

	NO: 9)	
451	APOC2 (SEQ ID NO: 2)	ATTTTAAGGCGTGTTAGT (SEQ ID NO: 1298)
452	APOC2 (SEQ ID NO: 2)	ATTTTAAGGTGTGTTAGT (SEQ ID NO: 1299)
453	APOC2 (SEQ ID NO: 2)	TGTCGGAGGCGAATTTT (SEQ ID NO: 1300)
454	APOC2 (SEQ ID NO: 2)	TGTTGGAGGTGAATTTT (SEQ ID NO: 1301)
455	APOC2 (SEQ ID NO: 2)	TTGGGGGACGTTATTGTT (SEQ ID NO: 1302)
456	APOC2 (SEQ ID NO: 2)	TTGGGGGATGTTATTGTT (SEQ ID NO: 1303)
457	APOC2 (SEQ ID NO: 2)	TGGGTTTGC GGAGAATGG (SEQ ID NO: 1304)
458	APOC2 (SEQ ID NO: 2)	TGGGTTTGTGGAGAATGG (SEQ ID NO: 1305)
459	CACNA1G (SEQ ID NO: 3)	GGTCGAGTCGATAAAAGTTT (SEQ ID NO: 1306)
460	CACNA1G (SEQ ID NO: 3)	GGTTGAGTTGATAAAAGTTT (SEQ ID NO: 1307)
461	CACNA1G (SEQ ID NO: 3)	TTACGTGTTTAAGTACGAAG (SEQ ID NO: 1308)
462	CACNA1G (SEQ ID NO: 3)	TTATGTGTTTAAGTATGAAG (SEQ ID NO: 1309)
463	CACNA1G (SEQ ID NO: 3)	GAATTGATTCTGGGAGTAT (SEQ ID NO: 1310)
464	CACNA1G (SEQ ID NO: 3)	GAATTGATTCTGGGAGTAT (SEQ ID NO: 1311)
465	CACNA1G (SEQ ID NO: 3)	TAGGTTCGTTTAGAGTTG (SEQ ID NO: 1312)
466	CACNA1G (SEQ ID NO: 3)	TAGGTTTGTTTAGAGTTG (SEQ ID NO: 1313)

467	EGR4 (SEQ ID NO: 4)	GGAAGCGTATTTATCGGA (SEQ ID NO: 1314)
468	EGR4 (SEQ ID NO: 4)	GGAAGTGTATTTATTGGA (SEQ ID NO: 1315)
469	EGR4 (SEQ ID NO: 4)	AGGCGTAGCGTTTATAGAT (SEQ ID NO: 1316)
470	EGR4 (SEQ ID NO: 4)	AGGTGTAGTGTTTATAGAT (SEQ ID NO: 1317)
471	EGR4 (SEQ ID NO: 4)	TAACGTTATAGTTCGAGTTT (SEQ ID NO: 1318)
472	EGR4 (SEQ ID NO: 4)	TAATGTTATAGTTTGAGTTT (SEQ ID NO: 1319)
473	AR (SEQ ID NO: 5)	AGAGGTTGCGTTTATAGAG (SEQ ID NO: 1320)
474	AR (SEQ ID NO: 5)	AGAGGTTGTGTTTATAGAG (SEQ ID NO: 1321)
475	AR (SEQ ID NO: 5)	TTATAGTCGTAGTCGGTTT (SEQ ID NO: 1322)
476	AR (SEQ ID NO: 5)	TTATAGTTGTAGTTGGTTT (SEQ ID NO: 1323)
477	AR (SEQ ID NO: 5)	TTATTTTCGAGAGAGGTTG (SEQ ID NO: 1324)
478	AR (SEQ ID NO: 5)	TTATTTTGAGAGAGGTTG (SEQ ID NO: 1325)
479	AR (SEQ ID NO: 5)	GTCGTGGTCGTTAGTAAG (SEQ ID NO: 1326)
480	AR (SEQ ID NO: 5)	GTTGTGGTTGTTAGTAAG (SEQ ID NO: 1327)
481	AR (SEQ ID NO: 5)	AGTATTTTCGGACGAGGA (SEQ ID NO: 1328)
482	AR (SEQ ID NO: 5)	AGTATTTTGGATGAGGA (SEQ ID NO: 1329)
483	RB1 (SEQ ID NO: 4)	TATTAGATTCGGGATAGG (SEQ ID NO: 1330)

	NO: 6)	
484	RB1 (SEQ ID NO: 6)	TATTAGATTTTGGGATAGG (SEQ ID NO: 1331)
485	RB1 (SEQ ID NO: 6)	GTAGAAGTACGTTCCGGT (SEQ ID NO: 1332)
486	RB1 (SEQ ID NO: 6)	GTAGAAGTATGTTGGGT (SEQ ID NO: 1333)
487	RB1 (SEQ ID NO: 6)	GTATCGATTAGCGTTTGTAGT (SEQ ID NO: 1334)
488	RB1 (SEQ ID NO: 6)	GTATTGATTAGTGTTTTGTAGT (SEQ ID NO: 1335)
489	RB1 (SEQ ID NO: 6)	AAAGGCGTTATGTCGTTTA (SEQ ID NO: 1336)
490	RB1 (SEQ ID NO: 6)	AAAGGTGTTATGTTGTTTA (SEQ ID NO: 1337)
491	BRCA2 (SEQ ID NO: 60)	TATAAGTTCGCGTTGG (SEQ ID NO: 1338)
492	BRCA2 (SEQ ID NO: 60)	TTATAAGTTTGTGTTGGT (SEQ ID NO: 1339)
493	BRCA2 (SEQ ID NO: 60)	TATTCGAGGCGTAGTA (SEQ ID NO: 1340)
494	BRCA2 (SEQ ID NO: 60)	TATTGAGGTGTAGTAGA (SEQ ID NO: 1341)
495	BRCA2 (SEQ ID NO: 60)	TTATCGTCGTAAAAGAT (SEQ ID NO: 1342)
496	BRCA2 (SEQ ID NO: 60)	GATTATTGTGTGAAAAGAT (SEQ ID NO: 1343)
497	BRCA2 (SEQ ID NO: 60)	ATTCGTTTTAGAGGCGTA (SEQ ID NO: 1344)
498	BRCA2 (SEQ ID NO: 60)	ATTGTTTTAGAGGTGTA (SEQ ID NO: 1345)
499	BRCA2 (SEQ ID NO: 60)	TAAGAAGTCGCGGTAG (SEQ ID NO: 1346)

500	BRCA2 (SEQ ID NO: 60)	GTAAGAAAGTTGTGGTAG (SEQ ID NO: 1347)
501	CCND1 (SEQ ID NO: 61)	TGTCGGCGTAGTAGTA (SEQ ID NO: 1348)
502	CCND1 (SEQ ID NO: 61)	TGTTGGTGTAGTAGTAG (SEQ ID NO: 1349)
503	CCND1 (SEQ ID NO: 61)	AGAAGCGAGAGTCGAG (SEQ ID NO: 1350)
504	CCND1 (SEQ ID NO: 61)	TAGAAGTGAGAGTTGAG (SEQ ID NO: 1351)
505	CCND1 (SEQ ID NO: 61)	TTTTAACGATCGGGT (SEQ ID NO: 1352)
506	CCND1 (SEQ ID NO: 61)	TTAATGATTGGGTGTTG (SEQ ID NO: 1353)
507	CCND1 (SEQ ID NO: 61)	TGTCGTTTATGCGGAA (SEQ ID NO: 1354)
508	CCND1 (SEQ ID NO: 61)	TGTTGTTTATGTGGAAG (SEQ ID NO: 1355)
509	CCND1 (SEQ ID NO: 61)	GGAAGATCGTCGTTAT (SEQ ID NO: 1356)
510	CCND1 (SEQ ID NO: 61)	AGATTGTTGTTATTTGGA (SEQ ID NO: 1357)
511	EDNRB (SEQ ID NO: 62)	GTTTTATTCGAGAAATGT (SEQ ID NO: 1358)
512	EDNRB (SEQ ID NO: 62)	TGTTTTATTGAGAAATGT (SEQ ID NO: 1359)
513	EDNRB (SEQ ID NO: 62)	GGAATGTTCTGTTTTA (SEQ ID NO: 1360)
514	EDNRB (SEQ ID NO: 62)	GGAATGTTGTGTTTTAT (SEQ ID NO: 1361)
515	EDNRB (SEQ ID NO: 62)	TAGGGGTCGATTTTAA (SEQ ID NO: 1362)
516	EDNRB (SEQ ID NO: 62)	TTAGGGGTTGATTTTAA (SEQ ID NO: 1363)

	NO: 62)	
517	EDNRB (SEQ ID NO: 62)	AATATAATCGGTTAGGTTA (SEQ ID NO: 1364)
518	EDNRB (SEQ ID NO: 62)	GATAATATAATTGGTTAGGT (SEQ ID NO: 1365)
519	EGFR (SEQ ID NO: 63)	AAGTTTTCGCGAGTTT (SEQ ID NO: 1366)
520	EGFR (SEQ ID NO: 63)	AAAGTTTTGTGAGTTT (SEQ ID NO: 1367)
521	EGFR (SEQ ID NO: 63)	GTATTATTTGACGTT (SEQ ID NO: 1368)
522	EGFR (SEQ ID NO: 63)	TATTTGGATGTTTGTA (SEQ ID NO: 1369)
523	EGFR (SEQ ID NO: 63)	TTTCGAGAGGGTTTCGTA (SEQ ID NO: 1370)
524	EGFR (SEQ ID NO: 63)	TTTGAGAGGGTTTGTA (SEQ ID NO: 1371)
525	EGFR (SEQ ID NO: 63)	ATTATTCGACGTTGGT (SEQ ID NO: 1372)
526	EGFR (SEQ ID NO: 63)	TTATTATTTGATGTTGGT (SEQ ID NO: 1373)
527	EGFR (SEQ ID NO: 63)	GTAAGTTCGCGGGGAT (SEQ ID NO: 1374)
528	EGFR (SEQ ID NO: 63)	GTAAGTTTGTGGGGAT (SEQ ID NO: 1375)
529	ERBB2 (SEQ ID NO: 64)	AGATCGCGTTATTGTT (SEQ ID NO: 1376)
530	ERBB2 (SEQ ID NO: 64)	AGAGATTGTGTTATTGTT (SEQ ID NO: 1377)
531	ERBB2 (SEQ ID NO: 64)	ATTTCGATTTCGGGGGA (SEQ ID NO: 1378)
532	ERBB2 (SEQ ID NO: 64)	AATTTATTTGGATTTGGG (SEQ ID NO: 1379)

533	ERBB2 (SEQ ID NO: 64)	GGATTTTTCGAGGAAAA (SEQ ID NO: 1380)
534	ERBB2 (SEQ ID NO: 64)	GGGATTTTTTGAGGAAA (SEQ ID NO: 1381)
535	ERBB2 (SEQ ID NO: 64)	TAGGTTTGC GCGAAGA (SEQ ID NO: 1382)
536	ERBB2 (SEQ ID NO: 64)	TTTGTGTGAAGAGAGG (SEQ ID NO: 1383)
537	FOS (SEQ ID NO: 65)	TTTCGGGTTTCGAGTAA (SEQ ID NO: 1384)
538	FOS (SEQ ID NO: 65)	TTTGGGTTTGAGTAATA (SEQ ID NO: 1385)
539	FOS (SEQ ID NO: 65)	TTTCGAAGGAATGCGTT (SEQ ID NO: 1386)
540	FOS (SEQ ID NO: 65)	TTTGAAGGAATGTGTT (SEQ ID NO: 1387)
541	FOS (SEQ ID NO: 65)	AGAAACGGTATCGAGT (SEQ ID NO: 1388)
542	FOS (SEQ ID NO: 65)	GGAGAAATGGTATTGAG (SEQ ID NO: 1389)
543	FOS (SEQ ID NO: 65)	AATTGTTTCGCGGGTTGTA (SEQ ID NO: 1390)
544	FOS (SEQ ID NO: 65)	AATTGTTTGTGGGTTGTA (SEQ ID NO: 1391)
545	NFKB1 (SEQ ID NO: 66)	TATAGGCGTTCGTTATT (SEQ ID NO: 1392)
546	NFKB1 (SEQ ID NO: 66)	GGATTATAGGTGTTTGTT (SEQ ID NO: 1393)
547	NFKB1 (SEQ ID NO: 66)	TATTACGTTTCGGTTAATT (SEQ ID NO: 1394)
548	NFKB1 (SEQ ID NO: 66)	ATTATGTTTGGTTAATTTT (SEQ ID NO: 1395)
549	NFKB1 (SEQ ID NO: 66)	AGTTATCGTATTCGGTT (SEQ ID NO: 1396)

	NO: 66)	
550	NFKB1 (SEQ ID NO: 66)	TGAGTTATTGTATTGGT (SEQ ID NO: 1397)
551	NFKB1 (SEQ ID NO: 66)	TTTAGITTTTCGGAGTTA (SEQ ID NO: 1398)
552	NFKB1 (SEQ ID NO: 66)	ITAGTTTTTGGAGTTAAA (SEQ ID NO: 1399)
553	NFKB1 (SEQ ID NO: 66)	AAAGGTCGATTGTTGG (SEQ ID NO: 1400)
554	NFKB1 (SEQ ID NO: 66)	TAAAGGTTGATTGTTGG (SEQ ID NO: 1401)
555	X51730 PGR (SEQ ID NO: 67)	TATCGAGAGGTTTCGAT (SEQ ID NO: 1402)
556	X51730 PGR (SEQ ID NO: 67)	TGTATTGAGAGGTTTGAT (SEQ ID NO: 1403)
557	X51730 PGR (SEQ ID NO: 67)	GAGTCGCGTGTATTATA (SEQ ID NO: 1404)
558	X51730 PGR (SEQ ID NO: 67)	AAAGGAGTTGTGTGTT (SEQ ID NO: 1405)
559	X51730 PGR (SEQ ID NO: 67)	AAATTGTCGTCGTAGT (SEQ ID NO: 1406)
560	X51730 PGR (SEQ ID NO: 67)	ATTAAATTGTTGTTAGT (SEQ ID NO: 1407)
561	X51730 PGR (SEQ ID NO: 67)	TGTCGTTTCGTTGGGATAA (SEQ ID NO: 1408)
562	X51730 PGR (SEQ ID NO: 67)	TGTTGTTTGTGGGATAA (SEQ ID NO: 1409)
563	TP53 (SEQ ID NO: 68)	TTTTACGACGGTGAT (SEQ ID NO: 1410)
564	TP53 (SEQ ID NO: 68)	TGTTTTTATGATGGTGA (SEQ ID NO: 1411)
565	TP53 (SEQ ID NO: 68)	GAAAATCGTTGGGGTT (SEQ ID NO: 1412)

566	TP53 (SEQ ID NO: 68)	GGAAAATTGTTGGGGT (SEQ ID NO: 1413)
567	TP53 (SEQ ID NO: 68)	AGTCGGTTTAAAGCGTA (SEQ ID NO: 1414)
568	TP53 (SEQ ID NO: 68)	AGTTGGTTTAAAGTGTAT (SEQ ID NO: 1415)
569	TP53 (SEQ ID NO: 68)	AGTTTCGGTTTCGTTAGA (SEQ ID NO: 1416)
570	TP53 (SEQ ID NO: 68)	AGTTTTGGTTTTGTTAGA (SEQ ID NO: 1417)
571	TP73 (SEQ ID NO: 69)	GTGCGAGTTAGTCGGA (SEQ ID NO: 1418)
572	TP73 (SEQ ID NO: 69)	GTGTGAGTTAGTTGGA (SEQ ID NO: 1419)
573	TP73 (SEQ ID NO: 69)	TATCGGTTTCGGAGTTA (SEQ ID NO: 1420)
574	TP73 (SEQ ID NO: 69)	AGGATATTGGTTTGGAG (SEQ ID NO: 1421)
575	TP73 (SEQ ID NO: 69)	AGAGTCGTTTCGGAATT (SEQ ID NO: 1422)
576	TP73 (SEQ ID NO: 69)	TGAGAGTTGTTTGAAT (SEQ ID NO: 1423)
577	ESR1 (SEQ ID NO: 70)	TTTTCGCGTTTATTTTAA (SEQ ID NO: 1424)
578	ESR1 (SEQ ID NO: 70)	TTTTTTGTGTTTATTTTAAAGT (SEQ ID NO: 1425)
579	ESR1 (SEQ ID NO: 70)	AGTAGATTTTCGTGCGTT (SEQ ID NO: 1426)
580	ESR1 (SEQ ID NO: 70)	AGTAGATTTTGTGTGTT (SEQ ID NO: 1427)
581	ESR1 (SEQ ID NO: 70)	AGTAGCGACGATAAGT (SEQ ID NO: 1428)
582	ESR1 (SEQ ID NO: 70)	TTAGTAGTGATGATAAGT (SEQ ID NO: 1429)

	NO: 70)	
583	ESR1 (SEQ ID NO: 70)	GATCGTTTTAAATCGAGT (SEQ ID NO: 1430)
584	ESR1 (SEQ ID NO: 70)	GGATTGTTTTAAATTGAGT (SEQ ID NO: 1431)
585	ESR1 (SEQ ID NO: 70)	TATCGGATTCGTAGGT (SEQ ID NO: 1432)
586	ESR1 (SEQ ID NO: 70)	TTTATTGGATTGTAGGTT (SEQ ID NO: 1433)
587	SERPINE1 (SEQ ID NO: 71)	AGTCGTGTATTATCGGA (SEQ ID NO: 1434)
588	SERPINE1 (SEQ ID NO: 71)	AGTTGTGTATTATTGGAG (SEQ ID NO: 1435)
589	SERPINE1 (SEQ ID NO: 71)	AGGCGGTCGGGTATAT (SEQ ID NO: 1436)
590	SERPINE1 (SEQ ID NO: 71)	AGGTGGTTGGGTATAT (SEQ ID NO: 1437)
591	SERPINE1 (SEQ ID NO: 71)	TAGAGTATCGGGTGGA (SEQ ID NO: 1438)
592	SERPINE1 (SEQ ID NO: 71)	AGAGTATTGGGTGGAT (SEQ ID NO: 1439)
593	SERPINE1 (SEQ ID NO: 71)	AGGATATTCGGGAGAG (SEQ ID NO: 1440)
594	SERPINE1 (SEQ ID NO: 71)	AGGATATTTGGGAGAGA (SEQ ID NO: 1441)
595	CALM1 (SEQ ID NO: 72)	TGGCGTTCGTTTTATTAA (SEQ ID NO: 1442)
596	CALM1 (SEQ ID NO: 72)	TGGTGTGTTGTTTATTAAA (SEQ ID NO: 1443)
597	CALM1 (SEQ ID NO: 72)	AGTAGTATTCGAGTTAAAT (SEQ ID NO: 1444)
598	CALM1 (SEQ ID NO: 72)	AGTAGTATTTGAGTTAAATT (SEQ ID NO: 1445)

599	CALM1 (SEQ ID NO: 72)	TAGAGGACGAGGTAGT (SEQ ID NO: 1446)
600	CALM1 (SEQ ID NO: 72)	TAGAGGATGAGGTAGTT (SEQ ID NO: 1447)
601	CALM1 (SEQ ID NO: 72)	TTAGTTGTCGAGGAGA (SEQ ID NO: 1448)
602	CALM1 (SEQ ID NO: 72)	TTAGTTGTTGAGGAGA (SEQ ID NO: 1449)
603	CSNK2B (SEQ ID NO: 73)	TGATTTTCGAATTTTGGT (SEQ ID NO: 1450)
604	CSNK2B (SEQ ID NO: 73)	TGATTTTGAATTTTGGT (SEQ ID NO: 1451)
605	CSNK2B (SEQ ID NO: 73)	GAACGTTTTAGTGC GTT (SEQ ID NO: 1452)
606	CSNK2B (SEQ ID NO: 73)	GGAATGTTTTAGTGT GTT (SEQ ID NO: 1453)
607	CSNK2B (SEQ ID NO: 73)	GTGCGAATTAGTTC GTT (SEQ ID NO: 1454)
608	CSNK2B (SEQ ID NO: 73)	GTGTGAATTAGTTTT GTT (SEQ ID NO: 1455)
609	CSNK2B (SEQ ID NO: 73)	ATTTTCGGTTAATTC GTT (SEQ ID NO: 1456)
610	CSNK2B (SEQ ID NO: 73)	ATTTTGGTTAATTTGT TG (SEQ ID NO: 1457)
611	FGFR1 (SEQ ID NO: 74)	GTATTTTCGTTGGTTA AGT (SEQ ID NO: 1458)
612	FGFR1 (SEQ ID NO: 74)	GTGTATTTTGT TGGTTAA (SEQ ID NO: 1459)
613	FGFR1 (SEQ ID NO: 74)	ATGTGAACGAAGTTA AG (SEQ ID NO: 1460)
614	FGFR1 (SEQ ID NO: 74)	ATGTGAATGAAGTTA AGA (SEQ ID NO: 1461)
615	FGFR1 (SEQ ID NO: 74)	TATGTTTCGGGGAAGT (SEQ ID NO: 1462)

	NO: 74)	
616	FGFR1 (SEQ ID NO: 74)	TATGTTTTGGGGAAGTA (SEQ ID NO: 1463)
617	FGFR1 (SEQ ID NO: 74)	TATGATTCGTTTTTAAGA (SEQ ID NO: 1464)
618	FGFR1 (SEQ ID NO: 74)	AGTTATGATTGTTTTTAA (SEQ ID NO: 1465)
619	MKI67 (SEQ ID NO: 75)	TTGAGATCGCGTTATT (SEQ ID NO: 1466)
620	MKI67 (SEQ ID NO: 75)	AGTTGAGATTGTGTTATT (SEQ ID NO: 1467)
621	MKI67 (SEQ ID NO: 75)	AGGATCGTTTGAGTCGGG (SEQ ID NO: 1468)
622	MKI67 (SEQ ID NO: 75)	AGGATTGTTTGAGTTGGG (SEQ ID NO: 1469)
623	MKI67 (SEQ ID NO: 75)	AAATTCGTTAGGCGTG (SEQ ID NO: 1470)
624	MKI67 (SEQ ID NO: 75)	AATTGTAGGTGTGGT (SEQ ID NO: 1471)
625	MKI67 (SEQ ID NO: 75)	TGAGTTCGGGAGTTTA (SEQ ID NO: 1472)
626	MKI67 (SEQ ID NO: 75)	TTGAGTTTGGGAGTTTA (SEQ ID NO: 1473)
627	NPM1 (SEQ ID NO: 76)	AGTAGTATTCGTTTATTTT (SEQ ID NO: 1474)
628	NPM1 (SEQ ID NO: 76)	GAGTAGTATTTGTTTATTTT (SEQ ID NO: 1475)
629	NPM1 (SEQ ID NO: 76)	ATTTAAGTGCGTGTTGT (SEQ ID NO: 1476)
630	NPM1 (SEQ ID NO: 76)	ATTTAAGTGTGTGTTGT (SEQ ID NO: 1477)
631	NPM1 (SEQ ID NO: 76)	GTTTTTCGATGGAAGAT (SEQ ID NO: 1478)

632	NPM1 (SEQ ID NO: 76)	TGTTTTTTGATGGAAGAT (SEQ ID NO: 1479)
633	NPM1 (SEQ ID NO: 76)	TGATGGACGTGGATAT (SEQ ID NO: 1480)
634	NPM1 (SEQ ID NO: 76)	TTGATGGATGTGGATAT (SEQ ID NO: 1481)
635	MAPK1 (SEQ ID NO: 77)	AGTTTTACGTTTCGATT (SEQ ID NO: 1482)
636	MAPK1 (SEQ ID NO: 77)	TGTAGTTTTATGTTTTGAT (SEQ ID NO: 1483)
637	MAPK1 (SEQ ID NO: 77)	AAGAAACGATCGAATTT (SEQ ID NO: 1484)
638	MAPK1 (SEQ ID NO: 77)	AAATGATTGAATTGGGA (SEQ ID NO: 1485)
639	MAPK1 (SEQ ID NO: 77)	ATTTATTTTTCGTGTGTAT (SEQ ID NO: 1486)
640	MAPK1 (SEQ ID NO: 77)	AATTTATTTTGTGTGTAT (SEQ ID NO: 1487)
641	MAPK1 (SEQ ID NO: 77)	GTGTATCGTGTTTTAAT (SEQ ID NO: 1488)
642	MAPK1 (SEQ ID NO: 77)	TGTGTATTGTGTTTAAAT (SEQ ID NO: 1489)
643	SYK (SEQ ID NO: 78)	GAAGTTATCGCGTTGG (SEQ ID NO: 1490)
644	SYK (SEQ ID NO: 78)	AGAAGTTATTGTGTTGG (SEQ ID NO: 1491)
645	SYK (SEQ ID NO: 78)	GATCGATGCGGTTTAT (SEQ ID NO: 1492)
646	SYK (SEQ ID NO: 78)	GGGATTGATGTGGTTTA (SEQ ID NO: 1493)
647	SYK (SEQ ID NO: 78)	GTTCGGCGGGAGGAGA (SEQ ID NO: 1494)
648	SYK (SEQ ID NO: 78)	GTTTGGTGGGAGGAGA (SEQ ID NO: 1495)

	NO: 78)	
649	SYK (SEQ ID NO: 78)	AGTCGATTTTCGTTTAG (SEQ ID NO: 1496)
650	SYK (SEQ ID NO: 78)	TAGTTGATTTTGTTAGT (SEQ ID NO: 1497)
651	SYK (SEQ ID NO: 78)	GGAAGAGTCGCGGGTT (SEQ ID NO: 1498)
652	SYK (SEQ ID NO: 78)	GGAAGAGTTGTGGGTT (SEQ ID NO: 1499)
653	TK2 (SEQ ID NO: 79)	AAGTTTCGAGTGTGAT (SEQ ID NO: 1500)
654	TK2 (SEQ ID NO: 79)	AAGTTTGAGTGTGATG (SEQ ID NO: 1501)
655	TK2 (SEQ ID NO: 79)	TTAAGACGGTGGAGAT (SEQ ID NO: 1502)
656	TK2 (SEQ ID NO: 79)	TTTAAGATGGTGGAGA (SEQ ID NO: 1503)
657	TK2 (SEQ ID NO: 79)	GAATTACGGTGATGGT (SEQ ID NO: 1504)
658	TK2 (SEQ ID NO: 79)	GAATGAATTATGGTGATG (SEQ ID NO: 1505)
659	TK2 (SEQ ID NO: 79)	AGGTAATTGTCGATTAGA (SEQ ID NO: 1506)
660	TK2 (SEQ ID NO: 79)	AGGTAATTGTTGATTAGAT (SEQ ID NO: 1507)
661	TK2 (SEQ ID NO: 79)	GTGTGTTTTTCGTAAATA (SEQ ID NO: 1508)
662	TK2 (SEQ ID NO: 79)	GTGTGTTTTTGTAATAA (SEQ ID NO: 1509)
663	HSPB1 (SEQ ID NO: 80)	GTGTACGGTAGGGTA (SEQ ID NO: 1510)
664	HSPB1 (SEQ ID NO: 80)	GTGTATGGTAGGGTAT (SEQ ID NO: 1511)

665	HSPB1 (SEQ ID NO: 80)	AGTCGTGTTACGGTAG (SEQ ID NO: 1512)
666	HSPB1 (SEQ ID NO: 80)	AGTTGTGTTATGGTAGG (SEQ ID NO: 1513)
667	HSPB1 (SEQ ID NO: 80)	TTTTTTCGTTAAGGAAAG (SEQ ID NO: 1514)
668	HSPB1 (SEQ ID NO: 80)	TTTTTTTTGTTAAGGAAAG (SEQ ID NO: 1515)
669	TES (SEQ ID NO: 81)	TAGAAAGTCGGTTCGTG (SEQ ID NO: 1516)
670	TES (SEQ ID NO: 81)	AGAAGTTGGTTGTGG (SEQ ID NO: 1517)
671	TES (SEQ ID NO: 81)	GTCGTGGACGTTTAGA (SEQ ID NO: 1518)
672	TES (SEQ ID NO: 81)	GTTGTGGATGTTTAGA (SEQ ID NO: 1519)
673	TES (SEQ ID NO: 81)	GATTGGCGGCGGAAG (SEQ ID NO: 1520)
674	TES (SEQ ID NO: 81)	ATTGGGTGGTGGAAGT (SEQ ID NO: 1521)
675	TES (SEQ ID NO: 81)	TAGCGGAGTCGGAGGT (SEQ ID NO: 1522)
676	TES (SEQ ID NO: 81)	TAGTGGAGTTGGAGGT (SEQ ID NO: 1523)
677	TES (SEQ ID NO: 81)	AATTCGGTCGTGGGAT (SEQ ID NO: 1524)
678	TES (SEQ ID NO: 81)	AATTGGTTGTGGGAT (SEQ ID NO: 1525)
679	SDC4 (SEQ ID NO: 82)	TTGCGGGTTATACGAT (SEQ ID NO: 1526)
680	SDC4 (SEQ ID NO: 82)	TTGTGGGTTATATGATT (SEQ ID NO: 1527)
681	SDC4 (SEQ ID NO: 82)	GTGAATCGTGTTAAGAT (SEQ ID NO: 1528)

	NO: 82)	
682	SDC4 (SEQ ID NO: 82)	TGTGAATTGTGTTAAGAT (SEQ ID NO: 1529)
683	PITX2 (SEQ ID NO: 83)	AGTCGGGAGAGCGAAA (SEQ ID NO: 1838)
684	PITX2 (SEQ ID NO: 83)	AGTTGGGAGAGTGAAA (SEQ ID NO: 1839)
685	PITX2 (SEQ ID NO: 83)	AAGAGTCGGGAGTCGGA (SEQ ID NO: 1840)
686	PITX2 (SEQ ID NO: 83)	AAGAGTTGGGAGTTGGA (SEQ ID NO: 1841)
687	PITX2 (SEQ ID NO: 83)	GGTCGAAGAGTCGGGA (SEQ ID NO: 1842)
688	PITX2 (SEQ ID NO: 83)	GGTTGAAGAGTTGGGA (SEQ ID NO: 1843)
689	PITX2 (SEQ ID NO: 83)	ATGTTAGCGGGTCGAA (SEQ ID NO: 1530)
690	PITX2 (SEQ ID NO: 83)	TAGTGGGTTGAAGAGT (SEQ ID NO: 1531)
691	GPR37 (SEQ ID NO: 84)	TTTCGATAGCGTTGA (SEQ ID NO: 1532)
692	GPR37 (SEQ ID NO: 84)	TTTTGATAGTGTGATTT (SEQ ID NO: 1533)
693	GPR37 (SEQ ID NO: 84)	ATAGCGGAAGATCGGT (SEQ ID NO: 1534)
694	GPR37 (SEQ ID NO: 84)	ATAGTGGAAGATTGGTT (SEQ ID NO: 1535)
695	GPR37 (SEQ ID NO: 84)	TAGCGGGAATCGGAG (SEQ ID NO: 1536)
696	GPR37 (SEQ ID NO: 84)	TAGTGGGGAATTGGAG (SEQ ID NO: 1537)
697	GPR37 (SEQ ID NO: 84)	ATTTATTTTCGTTCCGGTA (SEQ ID NO: 1538)

698	GPR37 (SEQ ID NO: 84)	ATTTATTTTGTGGTA (SEQ ID NO: 1539)
699	GPR37 (SEQ ID NO: 84)	ATTCGGTAGTCGTAGT (SEQ ID NO: 1540)
700	GPR37 (SEQ ID NO: 84)	ATTTGGTAGTTGTAGTTT (SEQ ID NO: 1541)
701	FGF1 (SEQ ID NO: 85)	TATAGGTTTCGCGGATT (SEQ ID NO: 1542)
702	FGF1 (SEQ ID NO: 85)	TTATAGGTTTGTGGATTG (SEQ ID NO: 1543)
703	FGF1 (SEQ ID NO: 85)	ATTATTCGGGAATTTTGT (SEQ ID NO: 1544)
704	FGF1 (SEQ ID NO: 85)	TATTATTTGGGAATTTTGT (SEQ ID NO: 1545)
705	FGF1 (SEQ ID NO: 85)	AGTTTGTATCGAGAAGT (SEQ ID NO: 1546)
706	FGF1 (SEQ ID NO: 85)	TAGTTTGTATTGAGAAGT (SEQ ID NO: 1547)
707	FGF1 (SEQ ID NO: 85)	TAGTAACGGGGGTTAT (SEQ ID NO: 1548)
708	FGF1 (SEQ ID NO: 85)	TGTAGTAATGGGGGTT (SEQ ID NO: 1549)
709	FGF1 (SEQ ID NO: 85)	GATTTTTTCGGATGGTA (SEQ ID NO: 1550)
710	FGF1 (SEQ ID NO: 85)	ATTTTTTGGATGGTATAG (SEQ ID NO: 1551)
711	GRIN2D (SEQ ID NO: 86)	GAGAGTCGGGATGATT (SEQ ID NO: 1552)
712	GRIN2D (SEQ ID NO: 86)	GGAGAGTTGGGATGAT (SEQ ID NO: 1553)
713	GRIN2D (SEQ ID NO: 86)	AGAGATTCGATTGGA (SEQ ID NO: 1554)
714	GRIN2D (SEQ ID NO: 86)	AAGAGATTTGATTGGA (SEQ ID NO: 1555)

	NO: 86)	
715	GRIN2D (SEQ ID NO: 86)	TAGGGTCGAGATTGG (SEQ ID NO: 1556)
716	GRIN2D (SEQ ID NO: 86)	TTAGGGTTGAGATTGG (SEQ ID NO: 1557)
717	GRIN2D (SEQ ID NO: 86)	AGTGTGGCGAATATTG (SEQ ID NO: 1558)
718	GRIN2D (SEQ ID NO: 86)	GTGTGGTGAATATTGAA (SEQ ID NO: 1559)
719	CTSB (SEQ ID NO: 87)	TGGGATATTCGAGGAAT (SEQ ID NO: 1560)
720	CTSB (SEQ ID NO: 87)	GGATATTTGAGGAATTGA (SEQ ID NO: 1561)
721	CTSB (SEQ ID NO: 87)	TGATATGCGTTATGGTT (SEQ ID NO: 1562)
722	CTSB (SEQ ID NO: 87)	TTGATATGTGTATGGTT (SEQ ID NO: 1563)
723	CTSD (SEQ ID NO: 88)	TAGAGGGCGAGCGGTA (SEQ ID NO: 1564)
724	CTSD (SEQ ID NO: 88)	TAGAGGGTGAGTGGA (SEQ ID NO: 1565)
725	CTSD (SEQ ID NO: 88)	GGAGCGCGAAAGTTAT (SEQ ID NO: 1566)
726	CTSD (SEQ ID NO: 88)	TAGGGGAGTGTGAAAG (SEQ ID NO: 1567)
727	CTSD (SEQ ID NO: 88)	TAGGAGGTCGCGTAGG (SEQ ID NO: 1568)
728	CTSD (SEQ ID NO: 88)	TAGGAGGTTGTGTAGG (SEQ ID NO: 1569)
729	CTSD (SEQ ID NO: 88)	ATTCGTTTAGATTCGGG (SEQ ID NO: 1570)
730	CTSD (SEQ ID NO: 88)	ATTTGTTTAGATTGGGG (SEQ ID NO: 1571)

731	PLAUR (SEQ ID NO: 89)	GGTATAGCGGGAAGT (SEQ ID NO: 1572)
732	PLAUR (SEQ ID NO: 89)	GGTATAGTGGGAAGTAA (SEQ ID NO: 1573)
733	PLAUR (SEQ ID NO: 89)	ATTATATTTATCGTTAAAGT (SEQ ID NO: 1574)
734	PLAUR (SEQ ID NO: 89)	TATATTTATTGTTAAAGTTTTT (SEQ ID NO: 1575)
735	PLAUR (SEQ ID NO: 89)	AGAGCGATTGTTTCGGG (SEQ ID NO: 1576)
736	PLAUR (SEQ ID NO: 89)	AGAGTGATTGTTTGGG (SEQ ID NO: 1577)
737	PLAUR (SEQ ID NO: 89)	GGGTTTACGTTAGGA (SEQ ID NO: 1578)
738	PLAUR (SEQ ID NO: 89)	GGGTTTATGTTAGGAA (SEQ ID NO: 1579)
739	PSA (SEQ ID NO: 90)	TTTCGATTCGGTTTAGA (SEQ ID NO: 1824)
740	PSA (SEQ ID NO: 90)	AATTGTTTGGATTGGTT (SEQ ID NO: 1825)
741	PSA (SEQ ID NO: 90)	TAATGGGGCGTCGATT (SEQ ID NO: 1826)
742	PSA (SEQ ID NO: 90)	TTAATGGGGTGTGATT (SEQ ID NO: 1827)
743	PSA (SEQ ID NO: 90)	TATCGTAGCGTTAGG (SEQ ID NO: 1828)
744	PSA (SEQ ID NO: 90)	TATTGTAGTGTTAGGAA (SEQ ID NO: 1829)
745	PSA (SEQ ID NO: 90)	AGGAACGTTAGTCGTT (SEQ ID NO: 1830)
746	PSA (SEQ ID NO: 90)	TAGGAATGTTAGTTGTTT (SEQ ID NO: 1831)
747	PSA (SEQ ID NO: 90)	GGTCGTCGTATTATGGA (SEQ ID NO: 1832)

	NO: 90)	
748	PSA (SEQ ID NO: 90)	TGGTTGTGTATTATGGA (SEQ ID NO: 1833)
749	CGA (SEQ ID NO: 91)	ATATTTATTTTCGAAATTT (SEQ ID NO: 1580)
750	CGA (SEQ ID NO: 91)	TTATTTTGGAAATTTATAGT (SEQ ID NO: 1581)
751	CGA (SEQ ID NO: 91)	TGATTTGTCGTTATTATT (SEQ ID NO: 1582)
752	CGA (SEQ ID NO: 91)	TTGATTTGTTGTTATTATT (SEQ ID NO: 1583)
753	CGA (SEQ ID NO: 91)	TAAATTGACGTTATGGTA (SEQ ID NO: 1834)
754	CGA (SEQ ID NO: 91)	AAATTGATGTTATGGTAAA (SEQ ID NO: 1835)
755	CGA (SEQ ID NO: 91)	AATTGACGTTATGGTAAT (SEQ ID NO: 1836)
756	CGA (SEQ ID NO: 91)	TAAAAAATTGATGTTATGGT (SEQ ID NO: 1837)
757	CYP2D6 (SEQ ID NO: 92)	AAGTAGCGGTAAGGAT (SEQ ID NO: 1584)
758	CYP2D6 (SEQ ID NO: 92)	GAAGTAGTGGTAAGGAT (SEQ ID NO: 1585)
759	CYP2D6 (SEQ ID NO: 92)	TAGAGGGCGAAGGTTA (SEQ ID NO: 1586)
760	CYP2D6 (SEQ ID NO: 92)	AGAGGGTGAAGGTAT (SEQ ID NO: 1587)
761	CYP2D6 (SEQ ID NO: 92)	TGTATCGGTATTAACGTT (SEQ ID NO: 1588)
762	CYP2D6 (SEQ ID NO: 92)	TGTATTGGTATTAATGTTG (SEQ ID NO: 1589)
763	CYP2D6 (SEQ ID NO: 92)	GTACGTTATTCGTTAGG (SEQ ID NO: 1590)

764	CYP2D6 (SEQ ID NO: 92)	TGTATGTTATTTGTTAGGT (SEQ ID NO: 1591)
765	CYP3A4 (SEQ ID NO: 93)	AAAAGAGTCGTATAGAGA (SEQ ID NO: 1592)
766	CYP3A4 (SEQ ID NO: 93)	AAGAGTTGTATAGAGAGG (SEQ ID NO: 1593)
767	CYP3A4 (SEQ ID NO: 93)	GTGTGTCGGGAGTTATA (SEQ ID NO: 1594)
768	CYP3A4 (SEQ ID NO: 93)	GTGTGTTGGGAGTTATA (SEQ ID NO: 1595)
769	CYP3A4 (SEQ ID NO: 93)	AAATAGGCGATGTTTAA (SEQ ID NO: 1596)
770	CYP3A4 (SEQ ID NO: 93)	TAGAAATAGGTGATGTTT (SEQ ID NO: 1597)
771	CYP3A4 (SEQ ID NO: 93)	TAAAATTATAGCGTTTTTAA (SEQ ID NO: 1598)
772	CYP3A4 (SEQ ID NO: 93)	AAATTATAGTGTTTTTAAAT (SEQ ID NO: 1599)
773	TK1 (SEQ ID NO: 94)	AGGAATTCGGTACGTG (SEQ ID NO: 1600)
774	TK1 (SEQ ID NO: 94)	GAGGAATTTGGTATGTG (SEQ ID NO: 1601)
775	TK1 (SEQ ID NO: 94)	AATTACGAGTCGGTTT (SEQ ID NO: 1602)
776	TK1 (SEQ ID NO: 94)	GGTTAATTATGAGTTGGT (SEQ ID NO: 1603)
777	TK1 (SEQ ID NO: 94)	AGGTCGTTTCGTAGTA (SEQ ID NO: 1604)
778	TK1 (SEQ ID NO: 94)	TTAAGGTTGTTTTGTAGT (SEQ ID NO: 1605)
779	TK1 (SEQ ID NO: 94)	TTTCGGGAAGTTTACGAA (SEQ ID NO: 1606)
780	TK1 (SEQ ID NO: 94)	TTTGGAAGTTTATGAA (SEQ ID NO: 1607)

	NO: 94)	
781	RENBP (SEQ ID NO: 95)	TAGATTTTTCGGTTATTTT (SEQ ID NO: 1608)
782	RENBP (SEQ ID NO: 95)	TTTAGATTTTGGTTATTT (SEQ ID NO: 1609)
783	RENBP (SEQ ID NO: 95)	GGTTTATTCGAGTGGA (SEQ ID NO: 1610)
784	RENBP (SEQ ID NO: 95)	TGGTTATTTGAGTGGA (SEQ ID NO: 1611)
785	RENBP (SEQ ID NO: 95)	TAAAGTTTCGTTTAGGT (SEQ ID NO: 1612)
786	RENBP (SEQ ID NO: 95)	TTAAAGTTTGTGTTTAGGT (SEQ ID NO: 1613)
787	RENBP (SEQ ID NO: 95)	GGGATCGCGATTAATT (SEQ ID NO: 1614)
788	RENBP (SEQ ID NO: 95)	GGGATTGTGATTAATTTTG (SEQ ID NO: 1615)
789	F12 (SEQ ID NO: 96)	TGGATTAACGGACGGA (SEQ ID NO: 1616)
790	F12 (SEQ ID NO: 96)	TTGGATTAATGGATGGA (SEQ ID NO: 1617)
791	F12 (SEQ ID NO: 96)	GGACGGACGTTATGAG (SEQ ID NO: 1618)
792	F12 (SEQ ID NO: 96)	GGATGGATGTTATGAGG (SEQ ID NO: 1619)
793	F12 (SEQ ID NO: 96)	ATATTTTCGGTGAGTGT (SEQ ID NO: 1620)
794	F12 (SEQ ID NO: 96)	AATATTTTGGTGAGTGT (SEQ ID NO: 1621)
795	F12 (SEQ ID NO: 96)	GGGGGGTCGTTATTATA (SEQ ID NO: 1622)
796	F12 (SEQ ID NO: 96)	GGGGGGTTGTTATTATA (SEQ ID NO: 1623)

797	F12 (SEQ ID NO: 96)	GTTAGTTCGGAAGGT (SEQ ID NO: 1624)
798	F12 (SEQ ID NO: 96)	GGTTAGTTTGGAAGGT (SEQ ID NO: 1625)
799	REN (SEQ ID NO: 97)	TTATTGCGGGATAGAG (SEQ ID NO: 1626)
800	REN (SEQ ID NO: 97)	TTATTGTGGGATAGAGT (SEQ ID NO: 1627)
801	REN (SEQ ID NO: 97)	TTTTAGCGAGGTATTT (SEQ ID NO: 1628)
802	REN (SEQ ID NO: 97)	AGTTTTAGTGAGGTATT (SEQ ID NO: 1629)
803	REN (SEQ ID NO: 97)	GTTTGTGCGGAGATTA (SEQ ID NO: 1630)
804	REN (SEQ ID NO: 97)	TGTTGTGTTGGGAGATTA (SEQ ID NO: 1631)
805	REN (SEQ ID NO: 97)	TAATTATCGTTTAAAGGTG (SEQ ID NO: 1632)
806	REN (SEQ ID NO: 97)	TTAATTATTGTTTAAAGGTG (SEQ ID NO: 1633)
807	EBAG9 (SEQ ID NO: 98)	GTTTGACGTCGAGATT (SEQ ID NO: 1634)
808	EBAG9 (SEQ ID NO: 98)	TGATGTTGAGATTGGG (SEQ ID NO: 1635)
809	EBAG9 (SEQ ID NO: 98)	TTATCGGGAAATTCGTT (SEQ ID NO: 1636)
810	EBAG9 (SEQ ID NO: 98)	TTTTATTGGGAAATTTGTT (SEQ ID NO: 1637)
811	EBAG9 (SEQ ID NO: 98)	ATTTTATGTTTCGTTTATTT (SEQ ID NO: 1638)
812	EBAG9 (SEQ ID NO: 98)	TTAGTTTTGTTTATTTAAAG (SEQ ID NO: 1639)
813	MSMB (SEQ ID NO: 98)	ATTGGTATCGTTGAGG (SEQ ID NO: 1640)

	NO: 99)	
814	MSMB (SEQ ID NO: 99)	ATTGGTATTGTTGAGGT (SEQ ID NO: 1641)
815	MSMB (SEQ ID NO: 99)	TGTATAAAATCGAATAAGG (SEQ ID NO: 1642)
816	MSMB (SEQ ID NO: 99)	TGTATAAAATTGAATAAGGA (SEQ ID NO: 1643)
817	MSMB (SEQ ID NO: 99)	ATAGGGCGAAGGTTTA (SEQ ID NO: 1644)
818	MSMB (SEQ ID NO: 99)	ATAGGGTGAAGGTTTAG (SEQ ID NO: 1645)
819	X15323 angiotensinogen gene 5'-region and exon 1 (SEQ ID NO: 100)	TAGTTTCGGGAGATGT (SEQ ID NO: 1646)
820	X15323 angiotensinogen gene 5'-region and exon 1 (SEQ ID NO: 100)	TTAGTTTTGGGAGATGT (SEQ ID NO: 1647)
821	X15323 angiotensinogen gene 5'-region and exon 1 (SEQ ID NO: 100)	TAGGAGTCGGGGTTAA (SEQ ID NO: 1648)
822	X15323 angiotensinogen gene 5'-region and exon 1 (SEQ ID NO: 100)	TAGGAGTTGGGGTTAA (SEQ ID NO: 1649)
823	X15323 angiotensinogen. gene 5'-region and	AGTGAGTCGGTGTAGG (SEQ ID NO: 1650)

	exon 1 (SEQ ID NO: 100)	
824	X15323 angiotensinogen gene 5'-region and exon 1 (SEQ ID NO: 100)	GAGTGAGTTGGTGTAG (SEQ ID NO: 1651)
825	X15323 angiotensinogen gene 5'-region and exon 1 (SEQ ID NO: 100)	GAAGCGATATTACGTT (SEQ ID NO: 1652)
826	X15323 angiotensinogen gene 5'-region and exon 1 (SEQ ID NO: 100)	AGAAGTGATATTTATGTTG (SEQ ID NO: 1653)
827	ZNF147 (SEQ ID NO: 101)	TAGGTAACGTATAGAGAT (SEQ ID NO: 1654)
828	ZNF147 (SEQ ID NO: 101)	TTAGGTAATGTATAGAGA (SEQ ID NO: 1655)
829	ZNF147 (SEQ ID NO: 101)	AGGAGTGTCGTATTITA (SEQ ID NO: 1656)
830	ZNF147 (SEQ ID NO: 101)	AGGAGTGTGTATTTAG (SEQ ID NO: 1657)
831	ZNF147 (SEQ ID NO: 101)	AGGTTAGCGATTTTGA (SEQ ID NO: 1658)
832	ZNF147 (SEQ ID NO: 101)	AGGTTAGTGATTTTGAG (SEQ ID NO: 1659)
833	EBBP (SEQ ID NO: 102)	TTTAGGTCGTTTTATTAT (SEQ ID NO: 1660)
834	EBBP (SEQ ID NO: 102)	TTTAGGTTGTTTTATTATA (SEQ ID NO: 1661)
835	EBBP (SEQ ID NO: 102)	ATGGTATCGAGTCGTT (SEQ ID NO: 1662)

	NO: 102)	
836	EBBP (SEQ ID NO: 102)	TGGTATTGAGTTGTTTAT (SEQ ID NO: 1663)
837	EBBP (SEQ ID NO: 102)	GGAATGTTTCGTTAAGT (SEQ ID NO: 1664)
838	EBBP (SEQ ID NO: 102)	ATGTTTTGTTAAGTGGG (SEQ ID NO: 1665)
839	EBBP (SEQ ID NO: 102)	TTACGAGTGTGACGGA (SEQ ID NO: 1666)
840	EBBP (SEQ ID NO: 102)	TTATGAGTGTGATGGAT (SEQ ID NO: 1667)
841	CALR (SEQ ID NO: 103)	TGTTTTACGTTGTAGAA (SEQ ID NO: 1668)
842	CALR (SEQ ID NO: 103)	GTTTTATGTTGTAGAAAG (SEQ ID NO: 1669)
843	CALR (SEQ ID NO: 103)	AGAGGTACGTGATTGG (SEQ ID NO: 1670)
844	CALR (SEQ ID NO: 103)	TAGAGGTATGTGATTGG (SEQ ID NO: 1671)
845	CALR (SEQ ID NO: 103)	TTTTTTAATCGGTAAATGA (SEQ ID NO: 1672)
846	CALR (SEQ ID NO: 103)	TTTTTTAATTGGTAAATGAA (SEQ ID NO: 1673)
847	CALR (SEQ ID NO: 103)	AGATTGTAGTCGTTTTTT (SEQ ID NO: 1674)
848	CALR (SEQ ID NO: 103)	AGATTGTAGTTGTTTTTTT (SEQ ID NO: 1675)
849	CALR (SEQ ID NO: 103)	AGGTTTAACGATGTGAT (SEQ ID NO: 1676)
850	CALR (SEQ ID NO: 103)	AGGTTTAATGATGTGATT (SEQ ID NO: 1677)
851	BCAR1 (SEQ ID NO: 104)	AGTTTTCGATTAGCGTT (SEQ ID NO: 1678)

852	BCAR1 (SEQ ID NO: 104)	AGTTTTTGATTAGTGTTT (SEQ ID NO: 1679)
853	BCAR1 (SEQ ID NO: 104)	TGGCGAGTTTTTCGATTTA (SEQ ID NO: 1680)
854	BCAR1 (SEQ ID NO: 104)	TGGTGAGTTTTTGATTTA (SEQ ID NO: 1681)
855	BCAR1 (SEQ ID NO: 104)	TTTCGATTGTAGACGGT (SEQ ID NO: 1682)
856	BCAR1 (SEQ ID NO: 104)	TTTTGATTGTAGATGGTT (SEQ ID NO: 1683)
857	BCAR1 (SEQ ID NO: 104)	ATTATCGCGTGTTAT (SEQ ID NO: 1684)
858	BCAR1 (SEQ ID NO: 104)	GGTATTATTGTGTGTTTA (SEQ ID NO: 1685)
859	COX7A2L (SEQ ID NO: 105)	TTGTTCGAAGATCGTT (SEQ ID NO: 1686)
860	COX7A2L (SEQ ID NO: 105)	GTTGTTTGAAGATTGTTT (SEQ ID NO: 1687)
861	COX7A2L (SEQ ID NO: 105)	TAGCGTAAGGATTCGGT (SEQ ID NO: 1688)
862	COX7A2L (SEQ ID NO: 105)	TTAGTGTAAGGATTGGT (SEQ ID NO: 1689)
863	COX7A2L (SEQ ID NO: 105)	AGAGTTCGGTTTTTCGTA (SEQ ID NO: 1690)
864	COX7A2L (SEQ ID NO: 105)	AGAGTTTGTTTTTTGTA (SEQ ID NO: 1691)
865	COX7A2L (SEQ ID NO: 105)	ATTCGTATTTGCGGGTTA (SEQ ID NO: 1692)
866	COX7A2L (SEQ ID NO: 105)	ATTTGTATTTGTGGGTTA (SEQ ID NO: 1693)
867	AF174646 glandular kallikrein gene,	GTTCGTATAGCGTAGAT (SEQ ID NO: 1694)

	promoter region and partial sequence (SEQ ID NO: 106)	
868	AF174646 glandular kallikrein gene, promoter region and partial sequence (SEQ ID NO: 106)	GTTTGTATAGTGTAGATGT (SEQ ID NO: 1695)
869	AF174646 glandular kallikrein gene, promoter region and partial sequence (SEQ ID NO: 106)	AGAGGCGCGTTGTAGG (SEQ ID NO: 1696)
870	AF174646 glandular kallikrein gene, promoter region and partial sequence (SEQ ID NO: 106)	AGAGGTGTGTTGTAGG (SEQ ID NO: 1697)
871	AF174646 glandular kallikrein gene, promoter region and partial sequence (SEQ ID NO: 106)	TTGGGACGTGACGGGA (SEQ ID NO: 1698)
872	AF174646 glandular	TTGGGATGTGATGGGA (SEQ ID NO: 1699)

	kallikrein gene, promoter region and partial sequence (SEQ ID NO: 106)	
873	AF174646 glandular kallikrein gene, promoter region and partial sequence (SEQ ID NO: 106)	TAGGGGACGTACGTTT (SEQ ID NO: 1700)
874	AF174646 glandular kallikrein gene, promoter region and partial sequence (SEQ ID NO: 106)	TATTAGGGGATGTATGTT (SEQ ID NO: 1701)
875	KLK3 (SEQ ID NO: 107)	AATCGGGGATCGTATT (SEQ ID NO: 1702)
876	KLK3 (SEQ ID NO: 107)	AGAATTGCGGATTGTAT (SEQ ID NO: 1703)
877	KLK3 (SEQ ID NO: 107)	ATTTGTATTTCGGAGAGT (SEQ ID NO: 1704)
878	KLK3 (SEQ ID NO: 107)	TGTATTGGAGAGTTGT (SEQ ID NO: 1705)
879	AKR1B1 (SEQ ID NO: 108)	GTTTCGCGTGGTAGAA (SEQ ID NO: 1706)
880	AKR1B1 (SEQ ID NO: 108)	GTTTTGTGTGGTAGAAA (SEQ ID NO: 1707)
881	AKR1B1 (SEQ ID NO: 108)	GTTGCGCGAAGGAGTT (SEQ ID NO: 1708)
882	AKR1B1 (SEQ ID NO: 108)	GTTGTGTGAAGGAGTT (SEQ ID NO: 1709)

	ID NO: 108)	
883	AKR1B1 (SEQ ID NO: 108)	AGTTCGTGAGGTCGGTA (SEQ ID NO: 1710)
884	AKR1B1 (SEQ ID NO: 108)	AGTTTGTGAGGTTGGTA (SEQ ID NO: 1711)
885	AKR1B1 (SEQ ID NO: 108)	ATTTTCGTTTAGTACGGT (SEQ ID NO: 1712)
886	AKR1B1 (SEQ ID NO: 108)	GATTTTGTTTAGTATGGT (SEQ ID NO: 1713)
887	TGM4 (SEQ ID NO: 109)	TAATAAAATTTTCGGAATTTT (SEQ ID NO: 1714)
888	TGM4 (SEQ ID NO: 109)	TAATAAAATTTTGGAATTTT (SEQ ID NO: 1715)
889	TGM4 (SEQ ID NO: 109)	GGAAGGCGATGTTGAT (SEQ ID NO: 1716)
890	TGM4 (SEQ ID NO: 109)	GGAAGGTGATGTTGAT (SEQ ID NO: 1717)
891	TGM4 (SEQ ID NO: 109)	ATATAGTCGGTTTTTAGG (SEQ ID NO: 1718)
892	TGM4 (SEQ ID NO: 109)	TATAGTTGGTTTTTAGGG (SEQ ID NO: 1719)
893	TGM4 (SEQ ID NO: 109)	AGGTATTCGGTAGAGG (SEQ ID NO: 1720)
894	TGM4 (SEQ ID NO: 109)	AGGTATTGGTAGAGGT (SEQ ID NO: 1721)
895	AR (SEQ ID NO: 110)	AAGAGGCGAAAAGTAG (SEQ ID NO: 1722)
896	AR (SEQ ID NO: 110)	AAGAGGTGAAAAGTAGT (SEQ ID NO: 1723)
897	AR (SEQ ID NO: 110)	AGTAAGCGGTTGTATAT (SEQ ID NO: 1724)
898	AR (SEQ ID NO: 110)	AAAAGTAAGTGGTTGTAT (SEQ ID NO: 1725)

899	AR (SEQ ID NO: 110)	AAATTGAGCGTTTATGT (SEQ ID NO: 1726)
900	AR (SEQ ID NO: 110)	ATTGAGTGTTTATGTGTA (SEQ ID NO: 1727)
901	HSPA1A (SEQ ID NO: 111)	AGGCGTCGGGAGATTA (SEQ ID NO: 1728)
902	HSPA1A (SEQ ID NO: 111)	AGGTGTTGGGAGATTA (SEQ ID NO: 1729)
903	HSPA1A (SEQ ID NO: 111)	TTGCGTAATTTGGACGTT (SEQ ID NO: 1730)
904	HSPA1A (SEQ ID NO: 111)	TTGTGTAATTTGGATGTT (SEQ ID NO: 1731)
905	HSPA1A (SEQ ID NO: 111)	GTTTCGTTACGTTATAAT (SEQ ID NO: 1732)
906	HSPA1A (SEQ ID NO: 111)	GTTTGGTTATGTTATAATGG (SEQ ID NO: 1733)
907	HSPA1A (SEQ ID NO: 111)	TTGATATCGTTCGGTTA (SEQ ID NO: 1734)
908	HSPA1A (SEQ ID NO: 111)	TGTTGATATTGTTGGTTA (SEQ ID NO: 1735)
909	HSPA1A (SEQ ID NO: 111)	ATGGCGATGTTGATCGTT (SEQ ID NO: 1736)
910	HSPA1A (SEQ ID NO: 111)	ATGGTGATGTTGATTGTT (SEQ ID NO: 1737)
911	FKBP4 (SEQ ID NO: 112)	TTTATATTTTCGTCGTAGG (SEQ ID NO: 1738)
912	FKBP4 (SEQ ID NO: 112)	TTTTATATTTTGTGTAGG (SEQ ID NO: 1739)
913	FKBP4 (SEQ ID NO: 112)	ATGTCGGGAGATCGAT (SEQ ID NO: 1740)
914	FKBP4 (SEQ ID NO: 112)	GATGTTGGGAGATTGAT (SEQ ID NO: 1741)
915	FKBP4 (SEQ ID NO: 112)	AGGTCGTCGGGGAGAT (SEQ ID NO: 1742)

	NO: 112)	
916	FKBP4 (SEQ ID NO: 112)	AGGTTGTTGGGGAGAT (SEQ ID NO: 1743)
917	FKBP4 (SEQ ID NO: 112)	AGATTTCGAGTTCGAG (SEQ ID NO: 1744)
918	FKBP4 (SEQ ID NO: 112)	ATTTGAGTTTGAGGGT (SEQ ID NO: 1745)
919	ESR2 (SEQ ID NO: 113)	ATTTCGAGGATTACGTT (SEQ ID NO: 1746)
920	ESR2 (SEQ ID NO: 113)	ATTTGAGGATTATGTTT (SEQ ID NO: 1747)
921	ESR2 (SEQ ID NO: 113)	AGATGGCGTTTTTCGTA (SEQ ID NO: 1748)
922	ESR2 (SEQ ID NO: 113)	TAGATGGTGTTTTTTGTA (SEQ ID NO: 1749)
923	ESR2 (SEQ ID NO: 113)	ATTTTCGAATCGATTTT (SEQ ID NO: 1750)
924	ESR2 (SEQ ID NO: 113)	GGAGTATTTTGAATTGAT (SEQ ID NO: 1751)
925	ESR2 (SEQ ID NO: 113)	AGTTCGACGGTTTTAG (SEQ ID NO: 1752)
926	ESR2 (SEQ ID NO: 113)	AGGGAGTTTGATGGTT (SEQ ID NO: 1753)
927	ESR2 (SEQ ID NO: 113)	AGTTTACGTGATCGAG (SEQ ID NO: 1754)
928	ESR2 (SEQ ID NO: 113)	AGTTTATGTGATTGAGTT (SEQ ID NO: 1755)
929	IGF1 (SEQ ID NO: 114)	AGATTATGTCGAGTTGT (SEQ ID NO: 1756)
930	IGF1 (SEQ ID NO: 114)	AAGATTATGTTGAGTTGT (SEQ ID NO: 1757)
931	IGF1 (SEQ ID NO: 114)	TAGTATTCGGGTGATTT (SEQ ID NO: 1758)

932	IGF1 (SEQ ID NO: 114)	AGATAGTATTTGGGTGAT (SEQ ID NO: 1759)
933	IGF1 (SEQ ID NO: 114)	AGAAAGGACGATAAGAT (SEQ ID NO: 1760)
934	IGF1 (SEQ ID NO: 114)	AGAAAGGATGATAAGATT (SEQ ID NO: 1761)
935	VTN (SEQ ID NO: 115)	GGTGGTATCGATTGAT (SEQ ID NO: 1762)
936	VTN (SEQ ID NO: 115)	TGGTGGTATTGATTGAT (SEQ ID NO: 1763)
937	VTN (SEQ ID NO: 115)	TAGTGATTCGCGGGGA (SEQ ID NO: 1764)
938	VTN (SEQ ID NO: 115)	TAGTGATTTGTGGGGA (SEQ ID NO: 1765)
939	VTN (SEQ ID NO: 115)	TTATGTCGGAGGATGA (SEQ ID NO: 1766)
940	VTN (SEQ ID NO: 115)	ATTATGTTGGAGGATGA (SEQ ID NO: 1767)
941	VTN (SEQ ID NO: 115)	ATACGGTTTATGACGAT (SEQ ID NO: 1768)
942	VTN (SEQ ID NO: 115)	ATATGGTTTATGATGATGG (SEQ ID NO: 1769)
943	CTSL (SEQ ID NO: 116)	GGGTCGGGTGGACGAA (SEQ ID NO: 1770)
944	CTSL (SEQ ID NO: 116)	GGGTGGGTGGATGAA (SEQ ID NO: 1771)
945	CTSL (SEQ ID NO: 116)	TAAACGTGGGGTCGGG (SEQ ID NO: 1772)
946	CTSL (SEQ ID NO: 116)	TAAATGTGGGGTTGGG (SEQ ID NO: 1773)
947	CTSL (SEQ ID NO: 116)	GAGCGTTCGAGTTAAT (SEQ ID NO: 1774)
948	CTSL (SEQ ID NO: 116)	TTGGAGTGTTGAGTTA (SEQ ID NO: 1775)

	NO: 116)	
949	TGFB3 (SEQ ID NO: 117)	AGGACGAAGAAGCGGA (SEQ ID NO: 1776)
950	TGFB3 (SEQ ID NO: 117)	AGGATGAAGAAGTGGA (SEQ ID NO: 1777)
951	TGFB3 (SEQ ID NO: 117)	TAGGAAGCGTTGGTAA (SEQ ID NO: 1778)
952	TGFB3 (SEQ ID NO: 117)	TTTAGGAAGTGTGGTA (SEQ ID NO: 1779)
953	TGFB3 (SEQ ID NO: 117)	TAGTAGACGTGTAGAAG (SEQ ID NO: 1780)
954	TGFB3 (SEQ ID NO: 117)	AGTAGATGTGTAGAAGG (SEQ ID NO: 1781)
955	TGFB3 (SEQ ID NO: 117)	AGGTTGATCGTGGTAA (SEQ ID NO: 1782)
956	TGFB3 (SEQ ID NO: 117)	AGGTTGATTGTGGTAAA (SEQ ID NO: 1783)
957	MAPKAPK5 (SEQ ID NO: 118)	AGTAGTCGTTTTTCGGGA (SEQ ID NO: 1784)
958	MAPKAPK5 (SEQ ID NO: 118)	AGTAGTTGTTTTTTGGGA (SEQ ID NO: 1785)
959	MAPKAPK5 (SEQ ID NO: 118)	AATTCGGTAGTCGATG (SEQ ID NO: 1786)
960	MAPKAPK5 (SEQ ID NO: 118)	ATTTGGTAGTTGATGGA (SEQ ID NO: 1787)
961	MAPKAPK5 (SEQ ID NO: 118)	ATTCGGGGGAGGTCGAA (SEQ ID NO: 1788)
962	MAPKAPK5	ATTTGGGGGAGGTTGAA (SEQ ID NO: 1789)

	(SEQ ID NO: 118)	
963	MAPKAPK5 (SEQ ID NO: 118)	ATTACGGAATTCGGG (SEQ ID NO: 1790)
964	MAPKAPK5 (SEQ ID NO: 118)	TTATGGAATTTGGGG (SEQ ID NO: 1791)
965	PCAF (SEQ ID NO: 119)	GAGCGGTAGGTGTCGAA (SEQ ID NO: 1792)
966	PCAF (SEQ ID NO: 119)	GAGTGGTAGGTGTTGAA (SEQ ID NO: 1793)
967	PCAF (SEQ ID NO: 119)	TAAGATTTGCGGGTA (SEQ ID NO: 1794)
968	PCAF (SEQ ID NO: 119)	TGTAAGATTTGTGGGTA (SEQ ID NO: 1795)
969	PCAF (SEQ ID NO: 119)	AGTTCGTAGTTTCGAG (SEQ ID NO: 1796)
970	PCAF (SEQ ID NO: 119)	GTTTGTAGTTTGGAGGA (SEQ ID NO: 1797)
971	PCAF (SEQ ID NO: 119)	TAGGGCGCGGAGTAGA (SEQ ID NO: 1798)
972	PCAF (SEQ ID NO: 119)	TAGGGTGTGGAGTAGA (SEQ ID NO: 1799)
973	NCOA3 (SEQ ID NO: 120)	GATGATATTTGCGGATTA (SEQ ID NO: 1800)
974	NCOA3 (SEQ ID NO: 120)	GATGATATTTGGGATTAA (SEQ ID NO: 1801)
975	NCOA3 (SEQ ID NO: 120)	ATAGTTTCGTGGTTTTGAT (SEQ ID NO: 1802)
976	NCOA3 (SEQ ID NO: 120)	ATAGTTTGTGGTTTTGAT (SEQ ID NO: 1803)
977	NCOA3 (SEQ ID NO: 120)	TTAGTTCGTTTATTGAA (SEQ ID NO: 1804)

	NO: 120)	
978	NCOA3 (SEQ ID NO: 120)	TTTAGTTTGTGTTATTTGAAA (SEQ ID NO: 1805)
979	NCOA3 (SEQ ID NO: 120)	AGGATTCGTGTTTGTA (SEQ ID NO: 1806)
980	NCOA3 (SEQ ID NO: 120)	AGGATTGTGTTTGTA (SEQ ID NO: 1807)
981	PRKCD (SEQ ID NO: 121)	ATTTATTTTCGTTGTAGG (SEQ ID NO: 1808)
982	PRKCD (SEQ ID NO: 121)	TATTTATTTTGTGTAGG (SEQ ID NO: 1809)
983	PRKCD (SEQ ID NO: 121)	TTTCGGAACGGGAAT (SEQ ID NO: 1810)
984	PRKCD (SEQ ID NO: 121)	TAGTTTGGAAATGGGA (SEQ ID NO: 1811)
985	PRKCD (SEQ ID NO: 121)	GGACGGAGTTATCGGT (SEQ ID NO: 1812)
986	PRKCD (SEQ ID NO: 121)	GGATGGAGTTATTGTA (SEQ ID NO: 1813)
987	PRKCD (SEQ ID NO: 121)	GTTTAGCGGAGGGATA (SEQ ID NO: 1814)
988	PRKCD (SEQ ID NO: 121)	TGTTTAGTGGAGGGAT (SEQ ID NO: 1815)

Table 3. Predictive score for response^a.

Factor	<i>n</i>	<i>P</i>	OR ^b	(95% CI) ^c
Traditional factors-based score ^d , ($\chi^2=10.9$, 3 degrees of freedom)				

q1	50	0.013	1	
q2	50		1.51	(0.68-3.38)
q3	50		3.16	(1.40-7.15)
q4	50		2.90	(1.29-6.53)

Methylation-based score^e, ($\chi^2=44.3$, 3 degrees of freedom)

q1	50	<0.001	1	
q2	50		1.47	(0.62-3.47)
q3	50		5.52	(2.34-13.1)
q4	50		13.0	(4.97-33.8)

^a, Logistic regression was used to test the strength of a relationship of a factor with the type of response to tamoxifen treatment; ^b, Odds ratio; ^c, 95% confidence interval; ^d, Score based on multivariable analysis of the traditional factors age (>70 yr, 55-70 yr, 41-55 yr versus ≤40 yr)

5 dominant site of relapse (relapse to viscera or bone versus soft tissue), disease-free interval (>12 months versus ≤ 12 months), and log ER values. The score was divided into groups (q1 - q4) based on the 25th, 50th and 75th percentile values; ^e, Score based on the DNA methylation status of the 5 independent predicting genes PSA-T, STMN1, GRIN2D, TGFBR2 and S100A2. The score was divided into groups, q1 - q4, same as for the traditional factors-based

10 score.

Claims

1. A method for predicting the responsiveness of a subject with a cell proliferative disorder of the breast tissues to a therapy comprising one or more drugs which target the estrogen receptor pathway or are involved in estrogen metabolism, production, or secretion, said method comprising analysing the methylation pattern of a target nucleic acid comprising one or a combination of the genes taken from the group consisting of PSA, STMN1, S100A2, SFN, PRKCD, SYK, VTN, GRIN2D, TGFBR2 and COX7A2L and/or their regulatory regions by contacting at least one of said target nucleic acids in a biological sample obtained from said subject prior to or during treatment with the above mentioned substances.
2. A method according to Claim 1, wherein said target nucleic acid or acids comprise essentially one or more sequences from the group consisting of SEQ ID NOs: 27, 90, 41, 40, 121, 78, 115, 86, 43 and 105 and sequences complementary thereto.
3. A method according to Claims 1 or 2, wherein said cell proliferative disorder of the breast tissue is selected from the group consisting of ductal carcinoma *in situ*, lobular carcinoma, colloid carcinoma, tubular carcinoma, medullary carcinoma, metaplastic carcinoma, intraductal carcinoma *in situ*, lobular carcinoma *in situ* and papillary carcinoma *in situ*.
4. A method according to Claims 1 to 3, wherein said subjects are estrogen and/or progesterone receptor positive.
5. A method according to Claims 1 to 4, wherein said endocrine therapy is for the treatment of a relapse or metastatic cell proliferative disorder of the breast tissues.
6. A method according to claim 5, wherein said subjects have received chemotherapy.
7. A method according to claim 6, wherein said subjects did not receive chemotherapy.

8. A nucleic acid molecule consisting essentially of a sequence at least 18 bases in length according to one of the sequences taken from the group consisting of SEQ ID NOs: 188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586 and 587 and sequences complementary thereto.

9. An oligomer, in particular an oligonucleotide or peptide nucleic acid (PNA)-oligomer, said oligomer consisting essentially of at least one base sequence having a length of at least 10 nucleotides which hybridises to or is identical to one of the nucleic acid sequences according to SEQ ID NO:188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586 and 587.

10. The oligomer as recited in Claim 9, wherein the base sequence includes at least one CpG dinucleotide.

11. The oligomer as recited in Claim 10, characterised in that the cytosine of the CpG dinucleotide is located approximately in the middle third of the oligomer.

12. A set of oligomers, comprising at least two oligomers according to any of claims 9 to 11.

13. A set of oligomers as recited in Claim 12, comprising oligomers for detecting the methylation state of all CpG dinucleotides within the group of SEQ ID NO: 188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586 and 587 and sequences complementary thereto.

14. A set of at least two oligonucleotides as recited in one of Claims 9 through 13, which is used as primer oligonucleotides for the amplification of nucleic acid sequences of one of SEQ ID NO:188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586 and 587 and sequences complementary thereto.

15. A set of oligonucleotides as recited in one of Claims 9 through 13, characterised in that at least one oligonucleotide is bound to a solid phase.
16. Use of a set of oligonucleotides comprising at least three of the oligomers according to any of claims 9 through 15 for detecting the cytosine methylation state and/or single nucleotide polymorphisms (SNPs) within the sequences taken from the group SEQ ID NOs:188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586, 587 and sequences complementary thereto.
17. A method for manufacturing an arrangement of different oligomers (array) fixed to a carrier material for predicting breast cell proliferative disorders' response to tamoxifen treatment by analysis of the methylation state of any of the CpG dinucleotides of the group SEQ ID NOs:188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586, 587, wherein at least one oligomer according to any of the claims 9 through 15 is coupled to a solid phase.
18. An arrangement of different oligomers (array) obtainable according to claim 16.
19. An array of different oligonucleotide- and/or PNA-oligomer sequences as recited in Claim 18, characterised in that said oligonucleotides are arranged on a plane solid phase in the form of a rectangular or hexagonal lattice.
20. The array as recited in any of the Claims 18 or 19, characterised in that the solid phase surface is composed of silicon, glass, polystyrene, aluminium, steel, iron, copper, nickel, silver, or gold.
21. A DNA- and/or PNA-array for predicting breast cell proliferative disorders' response to a therapy comprising one or more drugs which target the estrogen receptor pathway or are involved in estrogen metabolism, production, or secretion by analysis of the methylation state of any of the CpG dinucleotides of the group SEQ ID NOs:188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364,

365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586, 587 comprising at least one nucleic acid according to one of the preceding claims.

22. A method according to any one of Claims 1 to 3 comprising the following steps:

- a) obtaining a biological sample containing genomic DNA,
- b) extracting the genomic DNA,
- c) converting cytosine bases in the genomic DNA sample which are unmethylated at the 5-position, to uracil or another base which is dissimilar to cytosine in terms of base pairing behavior;
- d) amplifying at least one fragment of the pretreated genomic DNA, wherein said fragments comprise one or more sequences selected from the group consisting of SEQ ID NO:188, 189, 430, 431, 314, 315, 542, 543, 214-217, 456-459, 556, 557, 376, 377, 618, 619, 364, 365, 606, 607, 306, 307, 548, 549, 220, 221, 462, 463, 344, 345, 586, 587 and sequences complementary thereto, and
- e) determining the methylation status of one or more genomic CpG dinucleotides by analysis of the amplificate nucleic acids.

23. The method according to Claim 22, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to SEQ ID NO: 1816-1833, 1114-1129, 1808-1815, 1762-1769, 1552-1559, 1490-1499, 1138-1147 and 1686-1693

24. The method as recited in Claim 22, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to Claims 9 through 15.

25. The method as recited in Claim 22, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to Claims 9 through 15 and extension of said hybridised oligonucleotide(s) by means of at least one nucleotide base.

26. The method as recited in Claim 22, characterised in that Step e) is carried out by means of sequencing.

27. The method as recited in Claim 22, characterised in that Step d) is carried out using methylation specific primers.

28. The method as recited in Claim 22, characterised in that Step e) is carried out by means of a combination of at least two of the methods described in Claims 23 through 27.

29. The method as recited in Claim 22, characterised in that the treatment is carried out by means of a solution of a bisulfite, hydrogen sulfite or disulfite.

30. A method according to any one of Claims 1 to 3 comprising the following steps:

- a) obtaining a biological sample containing genomic DNA,
- b) extracting the genomic DNA,
- c) digesting the genomic DNA comprising one or more of the sequences from the group consisting of SEQ ID NOs 27, 90, 41, 40, 121, 78, 115, 86, 43 and 105 and sequences complementary thereto with one or more methylation sensitive restriction enzymes, and
- d) determining of the DNA fragments generated in the digest of step c).

31. The method according to Claim 30, characterised in that the target sequence or sequences digested in Step c) comprises one or more sequences from the group consisting of SEQ ID NO 27, 90, 41, 40, 121, 78, 115, 86, 43 and 105.

32. A method according to one of Claims 30 or 31, wherein the DNA digest is amplified prior to step d).

33. The method as recited in one of Claims 22 through 29 and 32 characterised in that more than six different fragments having a length of 100 - 200 base pairs are amplified.

34. The method as recited in one of Claims 22 through 29, 32 and 33 characterised in that the amplification of several DNA segments is carried out in one reaction vessel.

35. The method as recited in one of the Claims 22 through 29 and 32 through 34, characterised in that the polymerase is a heat-resistant DNA polymerase.
- 5 36. The method as recited in one of the Claims 22 through 29 and 32 through 35, characterised in that the amplification is carried out by means of the polymerase chain reaction (PCR).
- 10 37. The method as recited in one of the 22 through 29 and 32 through 36, characterised in that the amplicates carry detectable labels.
38. The method according to Claim 37 wherein said labels are fluorescence labels, radionuclides and/or detachable molecule fragments having a typical mass which can be detected in a mass spectrometer.
- 15 39. The method as recited in one of the Claims 22 through 29, characterised in that the amplicates or fragments of the amplicates are detected in the mass spectrometer.
- 20 40. The method as recited in one of the Claims 38 and/or 39, characterised in that the produced fragments have a single positive or negative net charge for better detectability in the mass spectrometer.
- 25 41. The method as recited in one of Claims 37 through 40, characterised in that detection is carried out and visualised by means of matrix assisted laser desorption/ionization mass spectrometry (MALDI) or using electron spray mass spectrometry (ESI).
- 30 42. The method as recited in one of the Claims 22 through 37, characterised in that the genomic DNA is obtained from cells or cellular components which contain DNA, sources of DNA comprising, for example, cell lines, histological slides, biopsies, tissue embedded in paraffin, breast tissues, blood, plasma, lymphatic fluid, lymphatic tissue, duct cells, ductal lavage fluid, nipple aspiration fluid, bone marrow and combinations thereof.
43. A kit comprising a bisulfite (= disulfite, hydrogen sulfite) reagent as well as oligonucleotides and/or PNA-oligomers according to one of the Claims 9 through 15.

17-04-03

44. A kit according to claim 43, further comprising standard reagents for performing a methylation assay from the group consisting of MS-SNuPE, MSP, Methyl light, Heavy Methyl, nucleic acid sequencing and combinations thereof.

5
45. The use of a method according to one of claims 1 through 7, 17, and 20 to 42, a nucleic acid according to Claim 8, of an oligonucleotide or PNA-oligomer according to one of the Claims 9 through 15, of a kit according to Claim 43 or 44, of an array according to one of the Claims 19 through 21 or of a set of oligonucleotides according to one of claims 12 through 15 for the treatment, characterisation, classification and/or
10 differentiation, of breast cell proliferative disorders.

E30111

Abstract

5 The present invention relates to modified and genomic sequences, to oligonucleotides and/or PNA-oligomers for detecting the cytosine methylation state of genomic DNA, as well as to a method for predicting the response of a subject with a cell proliferative disorder of the breast tissues, to endocrine treatment.

Figure 1

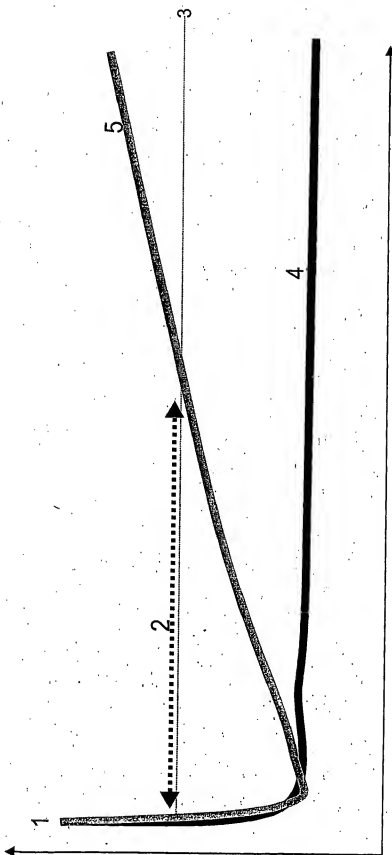
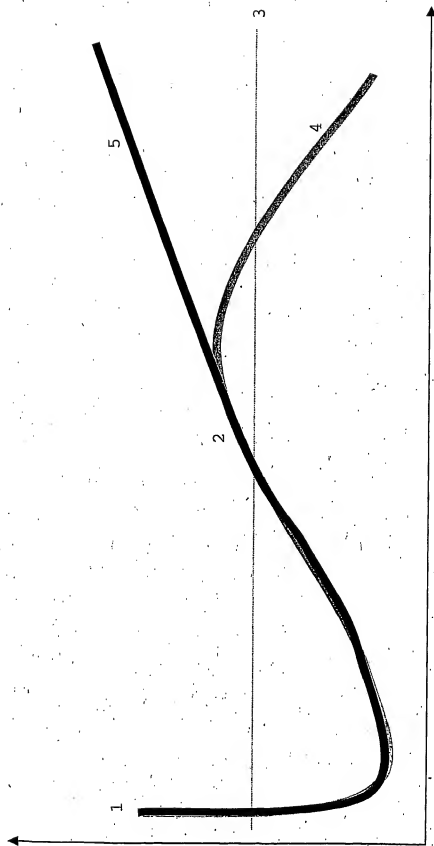


Figure 2



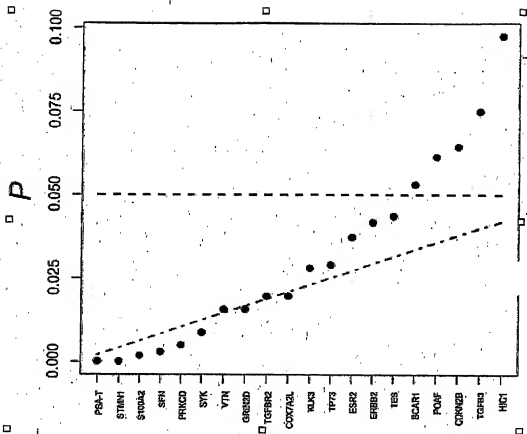


Figure 3

Figure 4

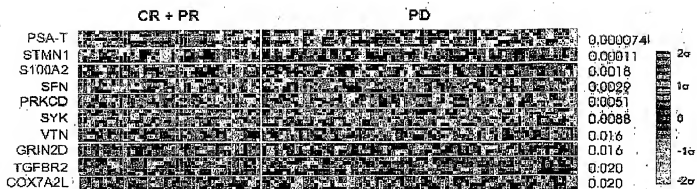
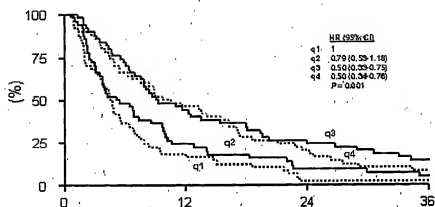
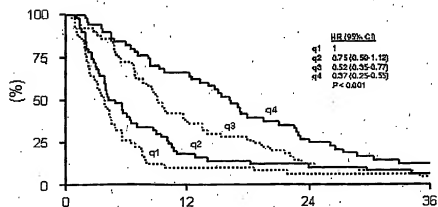


Figure 5

A



B



Sequence listing

<110> Epigenomics AG

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<210> 45

<211> 2501

<212> DNA

<213> Homo Sapiens

<400> 45

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<210> 46

<211> 2401

<212> DNA

<213> Homo Sapiens

<400> 46

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<211> 1508

<212> DNA

<213> Homo Sapiens

<400> 47

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<210> 48

<211> 1984

<212> DNA

<213> Homo Sapiens

<220>

<221> unsure

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<223> unknown base

<220>
 <221> unsure
 <222> (175, 207, 209, 214, 1181)
 <223> unknown base

<400> 48

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<213> Homo Sapiens

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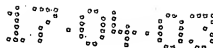
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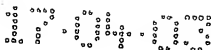
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<400> 94

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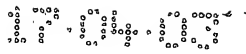
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12> DNA

13> Homo Sapiens

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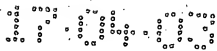


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 <213> Artificial Sequence



<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<212> DNA

<213> Artificial Sequence

<214> 0>

<223> chemically treated genomic DNA (Homo sapiens)

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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<223> unknown base

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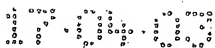
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<211> 6277

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<211> 1630

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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 <211> 1630
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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 3486

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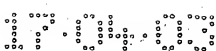
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<211> 2501

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<213> Artificial Sequence

<220>

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410

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 2501

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<213> Artificial Sequence



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<223> chemically treated genomic DNA (Homo sapiens)

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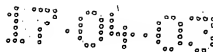
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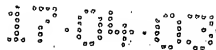
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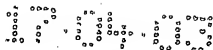
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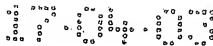
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<220>

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<220>
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 <222> (2526, 2669)
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<211> 3291

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<213> Artificial Sequence.

<220>

<223> chemically treated genomic DNA (Homo sapiens).

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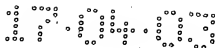
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 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 215

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 <211> 6558
 <212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<211> 6558

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens).

<400> 217

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<210> 225

<211> 2501

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 225

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<210> 226

<211> 2401

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 226

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<210> 227

<211> 2401

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 227

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<210> 228

<211> 1508

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 228

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<210> 229

<211> 1508

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 229

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<210> 230

<211> 1984

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<220>

<221> unsure

<222> (9, 17, 18, 33, 41, 49, 50, 52, 54, 62, 80, 84, 127, 157, 159)

<223> unknown base

<220>

<221> unsure

<222> (175, 207, 209, 214, 1181)

<223> unknown base

<400> 230

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<210> 231

<211> 1984

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<220>

<221> unsure

<222> (804, 1771, 1776..1778, 1810, 1826, 1828, 1858, 1901, 1905)

<223> unknown base

<220>

<221> unsure

<222> (1923, 1931, 1933, 1935, 1936, 1944, 1952, 1967, 1968, 1976)

<223> unknown base

<400> 231

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<210> 232

<211> 17897

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 232

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<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 234

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<210> 235

<211> 2987

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 235

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<210> 236

<211> 5683

<212> DNA

<213> Artificial Sequence

<220>

<223> Chemically treated genomic DNA (Homo sapiens)

<400> 236

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<211> 5683

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 237

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<220>

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<211> 4930

<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

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<220>

<223> chemically treated genomic DNA (Homo sapiens)

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 <211> 2501
 <212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 244

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<210> 245

<211> 2501

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 245

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<210> 246

<211> 3814

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 246

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<210> 247

<211> 3814

<212> DNA

<213> Artificial Sequence.

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 247

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<211> 2944

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

400> 254

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<210> 255

<211> 2944

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 255

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<210> 256

<211> 3862

<212> DNA

<213> Artificial Sequence

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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<210> 260

<211> 2501

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 260

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<210> 261
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 261

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<210> 262
<211> 3647
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 262

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<210> 263
 <211> 3647
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 263 .

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<210> 264

<211> 3050

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 264

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<210> 265

<211> 3050

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 265

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<210> 266

<211> 3397

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 266

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<210> 267

<211> 3397

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 267

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<211> 5087

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<211> 5087

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 269

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<211> 3077

<212> DNA

<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

<400> 272

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<211> 3077

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 273

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<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 274

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<210> 275

<211> 3814

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<210> 276

<211> 3223

<212> DNA

<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 276

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<211> 3223

<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 277

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<220>
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<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<211> 13076

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<220>

<221> unsure

<222> (1973, 2249, 2251, 9316)

<223> unknown base

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<211> 2451

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 284

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<211> 2451

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 285

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2451

<210> 286

<211> 3780

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 286

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<210> 287

<211> 3780

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 287

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<210> 288

<211> 2515

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 288

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<210> 289

<211> 2515

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 289

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<210> 290

<211> 3107

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 290

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<210> 291

<211> 3107

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 291

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<210> 292
 <211> 3283
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 292

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<210> 293

<211> 3283

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 293

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<400> 295

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a c g t a g g c g t	a t t t g g a g t c	c g c t a t a c g t	t t a t t a g c g	g t t a g a a a t t	g g t a t c g c g t	300
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a a t g c g c g g g	g g t c g g g c g c	g g g g g c g c g	t t c g t t a t g	t g t t t a g g t	t a g t t t t g a a	480
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<211> 3155

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<211> 14491

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<213> Artificial Sequence

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 <211> 5493
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<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 306

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<211> 5493

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens).

<400> 307

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<212> DN

<213> Artificial Sequence

 $\langle 220 \rangle$

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<211> 5605

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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<223> chemically treated genomic DNA (Homo sapiens)

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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 2972

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 319

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<211> 6101

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<211> 2425

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<220>

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<222> (289, 833, 1773, 2369, 2374, 2386)

<223> unknown base

<400> 322

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<211> 2425
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<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<20>
<221> unsure
<222> (40, 52, 57, 653, 1593, 2137)
<223> unknown base

<400> 323

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 <223> chemically treated genomic DNA (Homo sapiens)

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 <213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 325

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<211> 2474

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 326

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<211> 2474

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 327

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<211> 6175

<212> DNA

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<223> chemically treated genomic DNA (Homo sapiens)

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<212> DNA

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<213> Artificial Sequence

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<11> 2526

<12> DNA

<13> Artificial Sequence

<20>

<23> chemically treated genomic DNA (Homo sapiens)

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 <211> 2526
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

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<212> DNA
<213> Artificial Sequence

<220>
<223>, chemically treated genomic DNA (Homo sapiens)

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<211> 4022

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<222> (1005, 1015, 2239, 2651, 2724)

<223> unknown base

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<220>

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<221> unsure

<222> (1299, 1372, 1784, 3008, 3018)

<223> unknown base

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<210> 357

<211> 5387

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 357

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<223> chemically treated genomic DNA (Homo sapiens)

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<211> 3476

<212> DNA

<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<223> chemically treated genomic DNA (Homo sapiens)

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760

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<210> 370

<211> 3036

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 370

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<210> 371

<211> 3036

<212> DNA

<213> Artificial Sequence

<220>

<223> Chemically treated genomic DNA (Homo sapiens)

<400> 371

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<210> 372
 <211> 3091
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<220>
 <221> unsure
 <222> (2411, 2632, 2656)
 <223> unknown base

<400> 372

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<220>

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<222> (436, 460, 681)

<223> unknown base

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<211> 3083

<212> DNA

<213> Artificial Sequence

<220>

<223> Chemically treated genomic DNA (Homo sapiens)

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<211> 3083

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<223> chemically treated genomic DNA (Homo sapiens)

<400> 375

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<212> DNA

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<211> 2932

<212> DNA

<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 3720

<212> DNA

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<220>

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DATE 01-11-2001 BY 60322 UCBAW

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 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

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<211> 4316

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<223> chemically treated genomic DNA (Homo sapiens)

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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 396

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<210> 398

<211> 2240

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 398

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<210> 399

<211> 2240

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 399

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<210> 400

<211> 8169

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)
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 <221> unsure
 <222> (2047, 2136, 7481, 7492, 7502, 7503, 7505, 7511)
 <223> unknown base

<400> 400

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<220>

<223> chemically treated genomic DNA (Homo sapiens)

<220>

<221> unsure

<222> (659, 665, 667, 668, 678, 689, 6034, 6123)

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<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 1630

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 408

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<211> 5976

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<220>

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<211> 5976

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 411

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<211> 3486

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 412

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<211> 3486

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 413

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<210> 418

<211> 2501

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 418

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<210> 419

<211> 2501

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 419

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<220>
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<400> 420

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<400> 423.

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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 1631

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 428

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<211> 6680

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo. sapiens)

<400> 431

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<211> 1157

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 436

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<210> 437

<211> 1157

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 437

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<210> 438

<211> 8093

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<221> unsure

<222> (2526, 2669)

<223> unknown base

<400> 443

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<210> 444

<211> 3291

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 444

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gggtgaggtt	aggattttgt	tgtttttgg	aggattttaga	gttattgttta	ttgtgttttt	180
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<210> 445

<211> 3291

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 445

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gtttttgttt	gggggggaat	ttgggttggg	taggagatga	ggtttgtaat	atgtagggtt	180
taattaaaggg	tggaatagta	ttaagggttg	taaatattta	ttttggaag	agggataaagt	240
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<213> Artificial Sequence

<223> chemically treated genomic DNA (Homo sapiens)



tgt
tgt
ttg
ttt
gtg

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 447

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<210> 448

<211> 5203

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 448

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<210> 451

<211> 5087

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 451

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<211> 7110

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<213> Artificial Sequence

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<210> 457

<211> 2534

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 457

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<210> 458

<211> 6558

<212> DNA.

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 458

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<210> 459

<211> 6558

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 459

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<211> 1334

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 460

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<210> 461

<211> 1334

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 461

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<210> 462

<211> 5432

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<210> 467

<211> 2501

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 467

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<210> 468

<211> 2401

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 468

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<210> 469 "

<211> 2401

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 469

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<211> 1508

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 470

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<210> 471
<211> 1508
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 471

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<220>
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<220>
<221> unsure
<222> (9, 17, 18, 33, 41, 49, 50, 52, 54, 62, 80, 84, 127, 157, 159)
<223> unknown base

<220>
<221> unsure
<222> (175, 207..209, 214, 1181)
<223> unknown base

<400> 472

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<210> 473

<211> 1984

<212> DNA

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<223> unknown base

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<220>

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<210> 476

<211> 2987

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 476

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<210> 477

<211> 2987

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 477

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478

<211> 5683

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 478

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<210> 486

<211> 2501

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 486

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<210> 487
 <211> 2501
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 487

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<210> 488
 <211> 3814
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 488

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<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 489

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<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<211> 2944

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 496

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<210> 497

<211> 2944

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo, sapiens)

<400> 497

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<210> 498

<211> 3862

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 498

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<210> 503

<211> 2501

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 503

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<210> 504

<211> 3647

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 504

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<210> 505

<211> 3647

<212> DNA

<213> Artificial Sequence

<20>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 505

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<210> 506

<211> 3050

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 506

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<210> 507

<211> 3050

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 507

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<210> 508'

<211> 3397

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 508

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<210> 509

<211> 3397

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 509

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<213> Artificial Sequence

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<215> chemically treated genomic DNA (Homo sapiens)

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<211> 3077

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 514

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<210> 515

<211> 3077

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 515

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<210> 516

<211> 3814

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 516

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<210> 517
<211> 3814
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 517

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<210> 518

<211> 3223

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

70> 518

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<210> 519

<211> 3223

<212> DNA

<213> Artificial Sequence

<220>

<221> Chemically treated genomic DNA (Homo sapiens)

<400> 519

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<210> 520

<211> 5034

<212> DNA

<213> Artificial Sequence

<214> 520

<223> chemically treated genomic DNA (Homo sapiens)

<400> 520

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<211> 5034

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 521

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<210> 523

<211> 2942

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<213> Artificial Sequence

<220>

<23> chemically treated genomic DNA (Homo sapiens)

<400> 523

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<210> 526

<211> 2451

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 526

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<210> 527

<211> 2451

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 527

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<210> 528

<211> 3780

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 528

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<210> 529

<211> 3780

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 529

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 <211> 2515
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 <213> Artificial Sequence

<220>
 <223> chemically treated genomic DNA (Homo sapiens)

<400> 530

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<210> 531

<211> 2515

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 531

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<210> 532

<211> 3107

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens).

<400> 532

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<210> 533

<211> 3107

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 533

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<210> 534

<211> 3283

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 534

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<210> 535

<211> 3283

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 535

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<210> 536

<211> 3197

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 536

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<223> chemically treated genomic DNA (Homo sapiens)

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Copied from 10547741 on 04/15/2006

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<213> Artificial Sequence

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<211> 3155

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA. (Homo sapiens)

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<211> 14491

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<213> Artificial Sequence

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<211> 5605

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 551

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<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<211> 4394

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<211> 4857

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 555

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<223> chemically treated genomic DNA (Homo sapiens)

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<210> 561
<211> 2972
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 561

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<210> 562
<211> 6101

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens).

<400> 562

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<210> 563

<211> 6101

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 563

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<211> 2425

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<220>

<221> unsure

<222> (289, 833, 1773, 2369, 2374, 2386)

<223> unknown base

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<210> 565

<211> 2425

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<220>

<221> unsure

<222> (40, 52, 57, 653, 1593, 2137)

<223> unknown base

<400> 565

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<210> 566

<211> 2359

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<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<210> 567

<211> 2359

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 567

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gattttttt	tatttttttt	gttttttttag	gaagtttagat	agagtttgtt	gtggttttgt	240
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<210> 568

<211> 2474
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 568

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atttggttgt	tttgggtatt	taaagtgttg	ggattatagg	tgtgagttat	tatatattgt	180
tattttttgt	atatattgat	ggatatatag	aatagtttta	atttaattgt	ggaagatatt	240
atataagggg	atgaatttta	gggtggtgag	attaagtggg	gttgtttttg	aggttggtta	300
ttatagtatt	tttttatttt	ttttgttttg	tttgtttttg	tttttttatg	tgtagggttt	360
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<210> 569
<211> 2474
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 569

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<210> 570

<211> 6175

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 570

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<211> 1278

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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

<400> 577

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<223> chemically treated genomic DNA (Homo sapiens)

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 2526

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 583

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<222> (1299, 1372, 1784, 3008, 3018)

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<211> 5387

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 598

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<213> Artificial Sequence.

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<210> 601

<211> 4098

<212> DNA

<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 601

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<211> 13286

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 602

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<210> 612

<211> 3036

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 612

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<210> 613

<211> 3036

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 613

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<210> 614

<211> 3091

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<220>

<221> unsure

<222> (2411, 2632, 2656)

<223> unknown base

<400> 614

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<210> 615

<211> 3091

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<220>

<221> unsure

<222> (436, 460, 681)

<223> unknown base

<400> 615

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<210> 616

<211> 3083

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 616

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<210> 617

<211> 3083

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 617

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<210> 618

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<212> DNA

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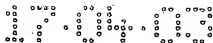
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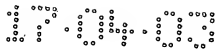
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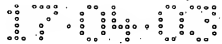
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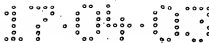
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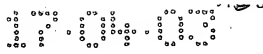
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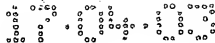
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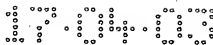
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